14

Bullous Diseases

essential

65

3

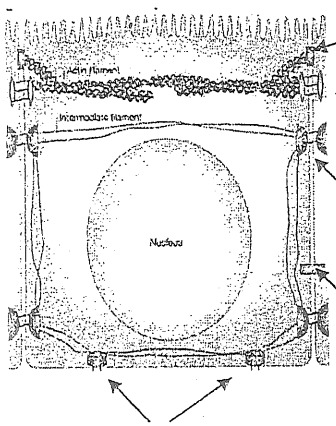
1. Basic: . Desmosome
   . Hemidesmosome & DEJ.
2. Autoimmune bullous diseases:
   . Intraepidermal blisters
   . Subepidermal blisters.
3. Non Autoimmune bullous diseases.

A. Basics

1. Structure of Desmosome:

. There are 5 Types of Cell (Keratinocyte) Junctions:

Five major categories of adhesion complexes are found in the epidermis.



Tight junctions – form at the apical end of lateral membranes forming extracellular diffusion barriers

Adherens Junctions – intercellular adhesion site linking actin cytoskeletal networks

Desmosomes – intercellular adhesion site linking keratin cytoskeletal networks

Gap Junctions – intercellular channels allowing diffusion of small molecules

Hemidesmosomes – adhesion site linking keratin cytoskeletal networks to extracellular matrix

. the Most important are:

1. Desmosome : Join KCs ē each other.
2. Hemidesmosomes : Join KCs ē l BMZ.

Structure of Desmosome

1. Inter Cellular Cement Substance (ICAM or Transmemb. proteins)
   ↓
   made up of Ca dependant Glycoproteins called: Cadherins

2. Attachement plaques (APs): (at inner side of cell memb.)

3. Cytoskeletal Pfn. (inside the cell)
   ↓
   Keratins. (Keratin intermediate filament) (KIF)

ڈیسموسوم کے اجزاء

Desmosome.

Adhesion complex	Transmembrane proteins (Cadherins)	Plaque proteins	Cytoskeletal proteins
Hemidesmosomes	integrin α6β4 BPAG2 (BP180)	BPAG1e (BP240) plectin	keratin
Desmonsomes (mediate slow)	desmoglein 1 desmoglein 3 desmocollin 1a, 1b desmocollin 2a, 2b desmocollin 3a, 3b	desmoplakin 1 & 2 Envp of Pers Plak. plakoglobin plakophilin keratoclamin	keratin
Adherens Junction (mediate quick but weak adhesion)	(1) E-cadherin P&E (1) Nectin	Catenins (α, β, p120) Afadin vinculin VASP p120ctn	actin
Tight Junction	JAMS claudins occludins	zona occludins 1, 2, 3 MAGIs 1, 2, 3	actin
Gap Junctions	connexins 15 human genes GJα, GJβ, GJγ families	-	-

Cadherins: 2 Types (یولوٹ)

(1) Classical Cadherins: E, P, N Cadherins they are cadherins of Adherens J.

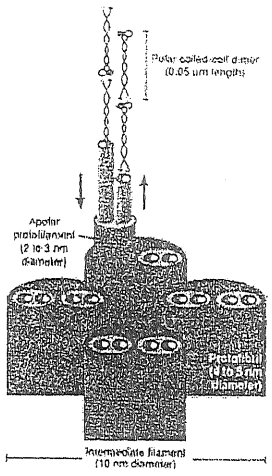
(2) Desmosomal Cadherins: DsG & DsG ہیں are Cadh. of Desmesomal Junct.

Keratins (KIF)

- Keratins are the structural unit of KCs.
- Present in the form of filaments inside the cell & have 2 ends:
  1. outer end: → attached to ⊥ Aps.
  2. Inner end: → Lies freely in ⊥ Cytoplasm towards the nucleus.

Keratins – gene family contains over 50 members

- mature keratin molecules have a diameter of 10-12 nm
- expressed in a tissue- and differentiation-specific manner
- keratins have conserved central rod domains and variable amino- and carboxy-terminal domains.
- Type I keratins are smaller and acidic; Type II keratins are larger, neutral/basic.
- keratin heterodimers further polymerize into larger filaments
- mutations that cause *major* defects in keratin molecular structure are non-viable
- mutations that cause *minor* defects in keratin molecular structure lead to major debilitating skin diseases.

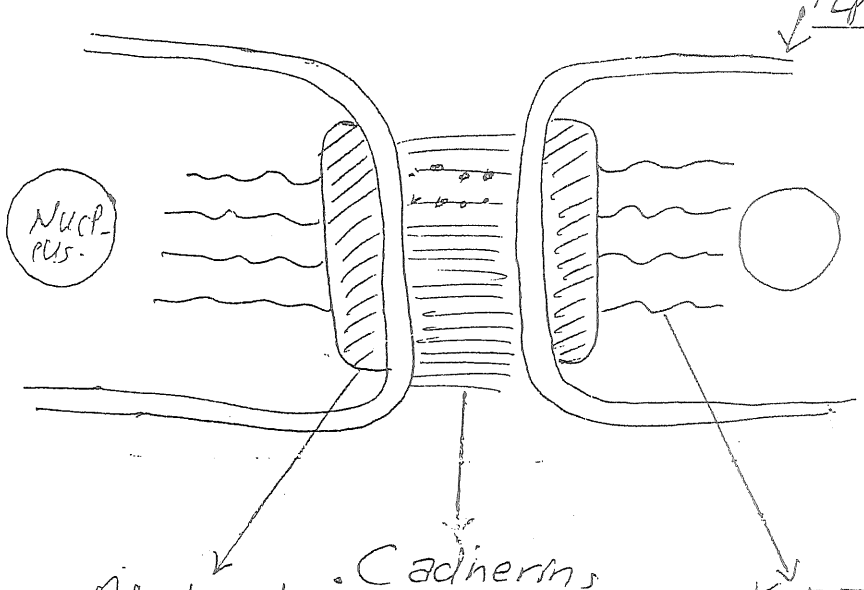


Tissue	Type I keratin expressed	Type II keratin expressed
✓ Basal cells	K14 (50 kD)	K5 (58 kD)
✓ Suprabasal cells	K10 (56.5 kD) K11 (56 kD)	K1 (67 kD) K2 (65 kD)
Hyperproliferative skin	K16 (48 kD)	K6 (56 kD)
Simple epithelia (also Merkel cells)	K18 (46 kD)	K8 (52 kD)

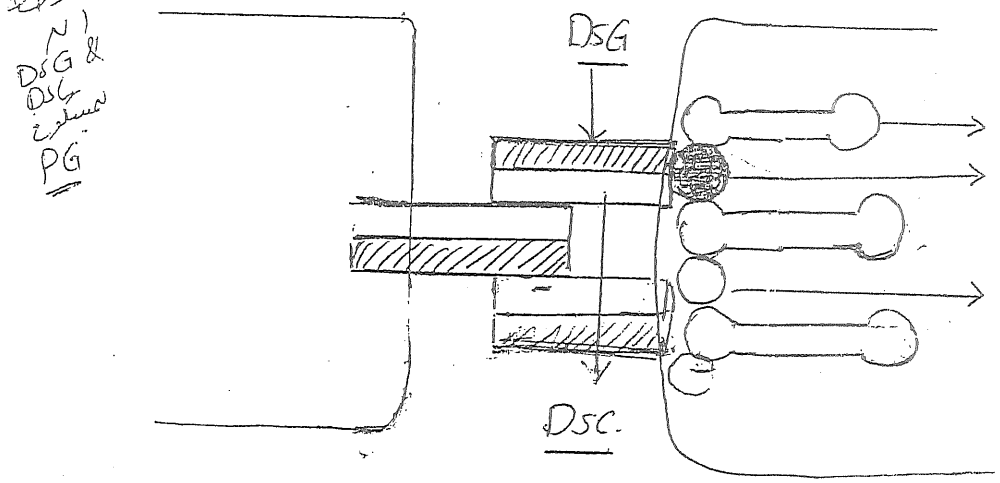
Genodermatoses Keratin mutation identified

Epidermolysis Bullosa Simplex K5, K14
Epidermolytic hyperkeratosis K1, K10
Palmoplantar keratoderma, epidermolytic K1, K9
Palmoplantar keratoderma, diffuse non-epidermolytic K1
Palmoplantar keratoderma, focal non-epidermolytic K16
Ichthyosis hystrix type Curth-Macklin K1

Non epiderm. ↓ K16



- Attachment plaques (APs)
  - Desmoplakin (1, 2)
  - plakoglobin
  - plakophillin I & II
  - Others: envoplakin & periplakin, Keratocalmin
- Cadherins
  - Desmoglein 1 2 3 4
  - Desmocollin:
    - 1 a&b
    - 2 a&b
    - 3 a&b
- KIF
  - Basal KCs → K5 & 14
  - Horny → K1 & 10
  - Prickle & granular: 2, 11 ع أنواع



- NB
  - DSG1 → is present in upper KG (More Superficial) So Autoantibodies against it → Superficial blisters [P.E, P.F]
  - DSG3 → in deeper KG (Suprabasal & Basal) Ab → More deeper blisters (PV, P. Vegetans)

- Skin Contains DsG I & III
- Neonatal skin & MM contains DsG III only

- Function of Desmosome: لبدنيا

1. Cellular stabilizat⊃ (adhesion)
2. Signaling centers: by controlling cytoplasmic part of signaling molecules (recently considered the mechanism of PV).
3. Plakoglobin: Has role in cellular prolif⊃ migrat⊃ & apoptosis.
4. Plakophillin: affect cytoplasm signaling pathways.

Bullous diseases

- Classification may be acc. to:

(1) Blister:
- Level
- Mechanism
- Infilterate

(2) disease Mechanism
- Immunological (Autoimmune)
- Non-Immunological (Non Autoimmune bullous)

- 1st Classification (dis. Mechanism or AEt.)

Immunobullous
- Epidermal Blistering diseases
  - Pemphigus family
- Subepid. Blistering diseases
  - Pemphigoid Family

non Immunobullous (4)
- EB
- SCPD
- H.H
- TAD (Groves)
- all (-ve DIF & IIF)

Skin & Mucosal Biopsy in Bullous diseases..

HP
- Vesicle
  - Early (To * bact. inf.)
  - Small
  - whole
  - area of intact skin
- Mucosal lesion → Edge of Erosion. (Intact vesicle)

DIF
- Perilesional Biopsy (Skin & MM)
- Immune deposits are degraded in Blistered skin → false -ve DIF

كخطوط عريضة

(3) Classification Acc. to level of Mechanism & Infilt. of Blister formation.

Epid. → 3 Levels

Sub epid. (See below) (3 levels)

① Subcorneal = Very Flaccid Blisters (ماشفتوش غير قشرة) ē Crust

ē

- **Acantholysis.**
  - 2 Pemphigus (Neut.)
    - Foliaceus واخواته (٣)
    - IgA (Neut) (SCPD Type)
- **Cytolysis** → SCPD (Neut.)
- **Spongiosis** → miliaria Crystallina (−ve)

- Others
  - Bullous impetigo (+ve)
  - SSSS (−Ve)
  - Pust. Ps (N), ETN (E), Candida (N), Impetigo Non-Bullous (N)

② Str. Spinosum = Intraepid. = "Flaccid Blisters"

- **Acantholysis.** → IgA pemph. (IEN type) (Neut)
- **Cytolysis** → Epidermolytic Hyperkeratosis (EHK)
- **Spongiosis** (Intercell. Edema)
  - Fungal inf.
  - Eczema.
  - TAD
  - Miliori Rubia
  - Incontinentia Pigmenti.
- **Intracellular edema** = Ballooning = Retic. degen. → Viral Blisters (HSV & VZV)

. EBS / Viral.

③ Suprabasal ⑥ "less Flaccid Blisters"

(All ē Acantholysis)

- 3 pemphigus → Eosinophilic Infilt.
  - Vulgaris
  - Vegetans
  - PNP
- 3 اسامي → "Scanty infiltrate" or (−Ve)
  - Dawier
  - Hailey-Hailey (BFP)
  - Grover (TAD)

"Pemphigus" (Greek pemphix = Blister or Bubbles)

- **Def.** →
  - Severe .. Even life threatening
  - Auto immune
  - Intra epid. blistering dis.
  - Ch. By < Acantholysis. / Auto antibodies against Epid. Cadherin's (family of Ca-dependant cell-cell adhesion molecules)

Classifications (أنواع)

(A) 4 Classical pemphigus

1. P. vulgaris → Subtype P. vegetans.
2. PNP
3. P. Foliaceus → subtypes < P. Erythematosus. / P. Herpetiformis. / Endemic foliaceus.
4. IgA pemphigus.

DIF (100% IC IgG ± C3)

(B) Other Variants:

1. Drug induced P.

2. Neonatal pemphigus

(Pemphigus Vulgaris)

- Age: Middle age (< 50 ys)
- Sex: M = F
- Race: More common among (Jewish.)
- Ass. HLA (A10, A26, BW38 & DR4)
- Clinically: Generalized flaccid blisters.
  - .. usually = Asympt or Tender > pruritic.
  - .. occur in NL skin → breaks easily → (denuded) areas that tend to ↑ in size & often become crusted
  - Post: .. Post. inflamm. Hyperpigm. usually present at site of Healed lesion ē usually (↓↓ By Time)
  - .. No scarring Except if 2ry bact. inf.

Sites

.. Skin: scalp, face, Trunk, axillae (Large amount of Pemph. Ag)

M.M .. affected in > 90% of cases.

- In 50-70%, The dis. start with mm affection before the skin. (مظهر مبكر للمرض)
- usually presented ē: oral, pharyngeal, nasal, conj. Erosions (Not blisters)

(Bad general condit.)

+Ve Both Nikol. & Asboe Hansen Signs But (not) diagnostic ...

.. Nikolsky's sign: firm / "sliding" press on unaffected skin → Avulsion of outermost epid. Layers from basal Layer & (±) blister formation.

- +Ve in: SJS / TEN & SSSS
- Indicates: Active dis.

Middle Age
lifelong
Threat.
Flaccid
Tender
NL skin
No scarring

Sheet
Skin
MM
Histopath.
Level & infilt)
Immunopath.
DIF - IIF
Antigen

HEMORRHAGIC CRUSTS OF THE VERMILION LIPS

- Herpes simplex
- Herpes zoster
- Pemphigus vulgaris
- Paraneoplastic pemphigus (see Fig. 23.6)
- Stevens–Johnson syndrome/TEN spectrum
- Erythema multiforme major (see Fig. 3.11)
- FDE

.L.P. CP

Asboe Hansen Sign: Linear (Lat.) pressure over the surface of (a recently) developed blister → Peripheral blister spreading.

(Bullae Spreading Phenomenon)

- **Histopathology** (Type 2)
  - suprabasal Acantholysis (with) Eosinophilic infiltration & +ve Tzanck smear (Acantholytic "Rounded up" Pemphigus cells in blister cavity)
  - The basal cell Layer forms a row of "Tombstone" that form the base of blister.

Immunopathology: (DIF أهم إختبار في التشخيص)

- DIF → 100% IC IgG + 50% C3, IgM (rare), IgA (±) (IgG4 doesn't fix complement)
  (Perilesional Skin) (Intercellular) (chicken wire at lower epid)
- IIF → 90% circulating IgG < 1/4 (more pathognomonic)

Pathogenesis

Target Antigens

- Desmosomal Ags
- Non Desmosomal Ags (HL)

Desmosomal Ags:

- DsG III:
  - (100%) of PV cases
  - present in Lower Epid. & MM (the Main DsG responsible for MM integrity)
  - Antibodies against it → Mucosal blisters & no or limited skin lesions (DsG I in skin Compensate).
- DsG I:
  - Attacked in 75% of PV cases.
  - present in all epidermis (sp.) + upper
  - Very little amount in MM (DsG III is the Main). ??

Non Desmosomal Ags:

- Acetyl Choline Receptors Pemphigus
- Annexin like (unknown pathogenic role).

- Anti DSG-I Antibodies → No oral lesions but subcorneal blisters (DSG3 compensate in MM)

This is called Compensation theory...

In PV: 2 Immunoresponses:

- 1ry response: Anti DSG III antibodies occurs first → Mucosal lesions at first
- 2ry response: Anti DSG III abs → exposure of previously sequestered epitopes → ++ Abs. product against DSG1 → 2ry Immune response → So both Anti DSG I & III are present → Skin lesions.

Skin lesions ظهرت بعد الـ oral lesions

- this called: "Epitope spreading theory"

NB: (1) Inactivation of DSG1 by staph. toxins (Exfoliative Toxins Can → bullous impetigo & SSSS simulating PF).

(2) Autoreactive T-cells may contribute to DSG3 attack by liberation of IL1 & TNF-α.

- Causes of death
  - Erosion → disturbed Epid. barrier → (Electrolyte Imbalance.
  - 2ry bact. inf.
  - Complications of Rx (e.g. Cs).

There are 2 Types of PV:

① Mucosal dominant: only Mucosal affect

② Muco Cut: Cut- & Mucosal affect

P. Vegetans

(Variant)

- **P. Vegetans:** Like P. Vulagaris in all things but differs in:

- Clinically, 2 Varieties:
  1. (Mild) = Pustular = Hallopeau type: "Pustular Eruption" (Pyoderma Vegetans) دايمي
  2. Severe = Blistering = Neumann type: P. Vulgaris like.

"تكمن بيدأ ب P. Vegetans أو بيدأ ب P. Vulgaris ويحصل تغير vegetans → P. Veget."

- the 2 types: → Crusted, Vegetating, Papillomatous proliferation (specially) on intertrigenous areas (also the scalp & Face).

DD
أقرب الأمراض له شكلاً
- H. Hailey
- Pemphigoid Vegetans
- Pyoderma Vegetans

(NB) - usually start as PV $\xrightarrow[\text{healing}]{\text{on}}$ verrucous changes & Hyperk. with pustules at the edge.

دارة - **Pathologically:**

- **Early:** as (PV)
  - Suprabasal Acantholysis
  - "Intraepid" Eosinophilic Microabscesses (hallmark)

- **Late:**
  - Hyperkeratosis
  - Acanthosis
  - Papillomatosis
  - Pseudoepitheliomatous Hyperplasia (PEH)

DIF, IIF, Targeted Ag & TTT as → PV.

(للعلم)

NB
1. P. Vegetans: may represent reactive pattern of skin to the autoimmune insult of P. Vulgaris.
2. vegetating lesions may develops on top of P. vulgaris lesions (ω are long standing & Resistant to TTT.) or develops de-novo.
3. (MM) may show "Cerebriform like lesions. (Invariable Involvement)

(DIF, IIF, Targeted Antigen & TTT → as P. Vulgaris)

Paraneoplastic pemphigus

" حاجة جامدة " (Arabic note, partly illegible)

onset of Tm:
- 70% at Diag. of PNP
- 30% after PNP

- Ass. with Bg or Mg Tms: Commonest:
  - Non-Hodgkins (40%)
  - Leukemia (Chr. lympho-cytic) (30%)
  - Castleman's Tm (10%)
  - Thymoma (6%)
  - Sarcoma (6%)
  - Waldenstrom's Macroglob. (6%)

Drugs: Fludarabine

- affect Elderly
- SKin: 5 varieties
  - P. vulgaris like: Flaccid bullae
  - B.P like: Tense bullae.
  - Targetoid lesions: EM like or TEN like (at PP)
  - Lichenoid lesions: Commonest in chronic Course > blistering.
  - GVHD: like.

MM (like ...) — 3 Ch: in all cases (100%), very Severe, Persistent (> PV)

- ulcerat° of:
  - Oropharynx → extend to Vermilion Border of lip. (PV)
  - Esophagus.
  - Conjunctiva → scarring.
  - Bronchioles → RD.

NB: Blisters & EM like lesions on (Palm & Soles) → differentiate bet PNP & P.V

- Histopath: mixture of:
  - suprabasal Acantholysis c̄ Eosinoph. Infilt. (PV like)
  - EM like (KC- Necrosis)
  - L.p like (lichenoid Infilt).
  - Interface Dermatitis (↓ + vacuolar deg.).

- DIF as PV
- IDIF (Rat Bladder 80% +ve) + Intracellular (AP) (Desmopl., plako.), Inter Cellular (DSG, DSC) & DEJ (BPAg 1, 2, plectin) deposit of IgG, C3, IgM, IgA. (Desmosome + DEJ)

. Targeted Antigen: تيجة

. DsGs (1&3) & Ds. Collins
. Desmoplakin, Plakoglobin, plakophillin, enveplakin
. BP Ag1 & BP Ag2, Plectin.

. Treatment:
  . if Bg Tm → disease Resolve if the Tm removed surgically
  . if Mg Tm: → the dis. usually Fetal ē in 2 Ys (Even) after ttt of underlying Mg.
    (d.t Sepsis, MoF, Resp. Failure)
    +
    o (choice) → Prednisone with or without:
      . Cyclophosphamide (Cytoxan)
      . Cyclosporine.

. MM: less responsive to ttt < skin.

Epi:
. Classical
. Localized
. Endemic
. Herpetiform

P. Foliaceus رقيقة

Course:
. chronic
. Better prognosis.

. Skin: . Very superficial blisters → Easily Eroded & Crusted (So: only Crust & Scales are seen) at (Face, scalp, upper Trunk)

. No st. Corneum or granulostum in MM so → No DsGI

Intact bullae مش بتشوفها
Crusted & Eroded بس بتشوف

. MM: rarely affected (very little DSG1).

. Path: . sub corneal blistering ē inflammatory cells in the cavity specially neutrophils
  (Subcorneal, Neut. Eos.)
  . upper dermal Eosinophilic infilt.

* Crusted & Scales هي اللي بتشوف
The Commonest bullous dis that may → Erythroderma.

- DIF & IIF → as P. vulgaris (but subcorneal deposits) → (upper epid.) (16)
- Targeted Ag: DsG1

P. foliaceous Varieties → P. Herpetiformis

- Localized → P. Erythematosus [Senear-Usher Syndrome]
  - crusted, scaly lesions on Seborrheic sites (Lupus like rash): malar area, face, interscapular & presternal
  - DIF: as P. vulgaris ± Deposits at DEJ (+ve LBT of un involved skin)
  - IIF: as P. vulgaris + ANA. (but -ve Antibs)
- Endemic (فوجو سيلفاجيم) [Fogo Selvagem]
  - CIP: (1) young children & adults (<20)
  - (2) d.t infectious agent Transmitted by Mosquito (Sim nigrimanum = Simulium sp.)
  - (3) CIP: . Erythroderma . Bullous . prurigo like.
  - (4) IH → moving to urban area (away from river)

- NB: the Term P. Erythematosus: was originally applied to patients having Immunologic features of Both diseases or patients have been reported to have the both. (+ANA; Inter Cell. dep.; DEJ dep.)

Pemphigus Herpetiformis:

- Clinically: Resemble (DH); pathologically: it is a Pemphigus (F or V)
- DIF & IIF
- Considered as: P.F variant (++) / P.V variant (+)
- Skin: Grouped Severely pruritic, Erythematous (vesicular, Bullous, Papular) Eruptions & Herpetiform Pattern
- Dapsone (DH)
- Mm: (±) [± DsG3]

- DIF: PV or PF
- IIF: " " "
- Ag: DsG1 > DsG3

IgA pemphigus

(Intercellular IgA dermatosis)

الملخص:
- 2 Types
- Sunflower at <
- IgA
- Desmocollin.
- Dapsone

. Skin : 2 Types < SCPD Type . / IEN Type. (Intra Epidermal Neutrophilic)

. Both types ch. by: Flacid vesicles or Pustules that tend to coalesce → annular or circinate pattern with crust in the center of lesion. that

has: **SunFlower like Pattern** → مميز جداً

at

Axillae & grion (b/w trunk & proximal Extrem. ± affected).

IgA bullous disease:
1. IgA pemphig
2. LABD
3. DH

Why Pustules: IgA → ++ Neut.

. MM: → rare

. Path: → < SCPD type: subcorneal Blisters. / IEN ": St. Spinosum Blistering

⊕ Neutrophilic infilt.

. DIF: IEN type: IgA deposition in < lower or entire Epid. / SCPD ": " " " " upper epid.

IIF: Circulating IgA autoantibs to Epith. cell surface

Diff. Form SCPD

. Targeted Ag (Heterogenous) < IEN → unknown ± → Other Ags: DsG1, DsG3 / SCPD → desmocollin 1

. Neonatal pemphigus:

. occurs as a complication of maternal pemphigus vulgaris (d.t. passage of IgG)

. C/p: → P. vulgaris

. Resolve ē catabolism of maternal Igs.

. Neonatal skin contain only DsG III (so mother ē PV is more dangerous in here term that PE).

Drug Related Pemphigus

(A) Drug induced (Non Antigenic / thiol drugs)

(B) Drug Triggered (Antigenic / Non thiol / Amide Drugs)

Induced Pemphigus (-SH)

(Non Antigenic) [thiol drugs]

- Drug play the 1st role.
- these drugs are:
  - Thiol drugs (sulfhydryl group).
  - Masked Thiols (Metabolized to thiol).

Furosemide (Lasix)
D. penicillamine
Captopril
piroxicam
Penicillin
Rifampicine

Mech. penicillamine & Captopril contain sulfahydryl group (SH) (thiol) that interact è Sulfhyl. group of DSG3 → ?? direct interfer è its adhesive funct → Acantholysis (cent ++ Ab. product)

Triggered Pemph

(Antigenic) [Non thiol]

- ! Drug play a (2nd) role.. it induces P. in presence of ! Major predisposing factors:
  - Endogenous
  - Genetic / Hereditary
  - Immunological

- These drugs as: "Non Thiol or Amide" group
  - Enal- & Eza pril
  - CCB

Mech.: the Drug acts as (hapten + Viral or bact. or endog. peptide → Form Ag → Autoab → attack DSG).

I.P.	11 ms	(4) ms
• CIP	40% → P. F. 30% → P. Vulg.	• P. Vulgaris or / • PE
M.M	18%	55%
Spontaneous resolut è in ≃ 6 ms. after Stop of Drugs.		• persist even after drug discontinuat.

Captopril & D-penicillamin → Commonest thiols

Drug Related Pemphigus

(A) Drug induced (Non Antigenic / Thiol drugs)

(B) Drug Triggered (Antigenic / Non thiol / Amide Drugs)

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- Drug play the 1st role.
- These drugs are:
  - Thiol drugs (sulfhydryl group).
  - Masked Thiols (Metabolized to thiol).
    - Furosemide (Lasix)
    - D. penicillamine
    - Captopril
    - piroxicam
    - Penicillin
    - Rifampicine

Mech. penicillamine & Captopril contain sulfahydryl group (SH) (thiol) that interact with (Sulfhyl) group of DSG3 → ?? direct interfere with adhesive Funct → Acantholysis (cont ++ Ab. products)

Triggered Pemph

(Antigenic) [Non thiol]

- Drug play a (2nd) role.. it induces P. in Presence of Major predisposing factors:
  - Endogenous
    - Genetic
    - Hereditary
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IP	11 ms	4 ms
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M.M	18%	55%
Spontaneous resolution in ≃ 6 ms. after Stop of Drugs.		• persist even after drug discontinuation.

Captopril & D-penicillamin → Commonest thiols

Treatment of Pemphigus

- **Basic rule:** • PV is a chronic, life long dis. with Exacerbat° & remission → so ## (IS) For Control Not For Cure (No Cure)

- **Aim of ##:**

(1) ↓ Antibody Synthesis:

- **Cyclophosphamide** → the most potent but has serious Toxicity
- **Cs** → relatively potent & rapid (≃ 2ms)
- other Immunosuppressives: less potent & Less rapid (4-5ms)

(2) physical removal of antibs: by plasma-pharesis.

(3) Induct° of Catabolism of antibs: IVIG.

(4) ↓↓ inflamm. e.g. Cs.

NB: • the antibs. once formed & reaches the SK in the development of dis. become inevitable. Their degradative halflife is ≃ 3ws

↓↓ Igs
- Existing → by degradat°
- Newly Formed → Immuno-Supp.

• improvement occurs only ē reduct° of both existing & newly formed antibodies → so improvement occurs very slowly unless Antbs. are physically removed (by pharesis) or by inducing their Catabolism (by IVIG).

• **Cs:** the Major Cause for morbidity & Mortality in PV if used in large doses.

• life long ##
1) life long ## (For control)
2) Combat° Therapy (Cs + others)

• ولذا فإن القاعدة العلاجية هي:

Use of Combinat° therapy:

Cs (to give Quick act°)
+
other immunosuppressive (steriod sparing to avoid Cs. S.E)

Lines of Ht

- **1s line therapy**
  - Systemic Cs
  - لازم نتبع معاها
  - "Steroid sparing" (2nd line)
- **2nd line**
  - Azath.
  - M M
  - MTX
  - Ciclosp.
  - Cyclo-phosph.
  - Chlor-ambucil
- **3nd line**
  - Nicotinamide
  - Tetracyclines
  - Trental
  - Dapsone
  - Salazopyrine
- (مهم) **Ht of ressistant cases**
  - Pulse Cs
  - Cyclophosphamid
  - IVIG
  - plasmapharesis
  - ECP
  - Biologics → (Rituximab)

Systemic Cs in PV.

- **Continous oral Cs** (1st line)
- (مهم) **Pulse steriod** (2nd line)
  - rapid control
  - no need for long term Ht
  - So ↓ S.E.
  - [illegible] • **IV Methyl prednisolone pulse**
    - 1gm IV drip over 2-3 hs for 3-5 days
    - ± repeated every 2-3 ws if needed.
    - (Over 3 hs for 3 ds, 1 3w)
    - [under cardiac monitoring].
    - داسوي
  - ([illegible]) **IV/IM Dexamethasone**
    - 100 mg daily for 3 ds / month.

Pulse (CDP): Cyclo → 500 mg/month; Dexa. pulse

Most Recent Regimen:

يحفظ جيدا
100 – 120 mg / day

1 – 1.5 mg / kg / d prednisolone for:

2 – 3 ws (or 6 – 8 ws)
غالبا خلال هذه الفترة يحدث تحسن

→ خلال هذه الفترة هانضيف
- Azathioprine
- MM

Improvement

(if clinical & Lab.)

↓

> CS نسحب ال
قد إيه ؟؟
وكل إيه ؟؟

- withdrawal every 2 – 4 ws
(in less serious dis (1 – 2 ws))

طريقة السحب:
- 100 — 60 mg —(بسحب)→ 20 mg decrements
- 60 — 20 mg → 10 mg " " "

↓

at 20 mg
There is 2 methods
for withdrawal

No improvement

↓

Consider resistant case e.g.
- plasmapharesis
- IVIG
- Rituximab. (375 mg / m² once weekly for 4 weeks)

Classical Method (1 2 – 4 ws)

- 20 — 10 (بسحب) 5 mg
في الأمراض الخطيرة
- < 10 mg (بسحب By) 2.5 mg (or better 1 mg)

till 5 mg → Then Measure serum Cortisol level; if > 10 ug/dl

; so HPA is functioning →

Stop Cs. or in Serious life long diseases (PV) → كمل لنهاية

Alternate day therapy

(day on, day off)

لازم عند جرعة (20 – 30)

(طريقتين)

[A] - 20 – 20 then 40 – 0
ونقلل الجرعة من ال day on
بمقدار 5 مجم كل مرة

أو

[B] - 20 – 20 → 25 – 15 then → 30 – 10 then → 35 – 5 → 40 – 0
(نزيد الجرعة على ال day on بمقدار 5 مجم ونقلل 5 مجم من ال day off)

Alternate day regimen:

- لما نوصل ل 20 – 30 مجم
- لازم الجرعة تكون صباحا ✓
- نقلل نصيا NSAIDs أو نعطي شيء مع ال Cs
- اشتكاء مش يحصل day off withdrawal symptoms.

- Better release of:
  - HPA
  - CMI
  - WBCs
  - K^+ exc

Assessment of response or improvement

1. Clinical (كل أسبوع)
   - Healing of old lesions
   - absence of new lesions.
2. lab: ↓↓ Ig titer. (IDIF)

NB on Cs:

A. Mechanism of Act⊃:

1. Anti inflammatory
2. Ig (↓ synth. & ↑ Catabolism).
3. # Macrophage Funct⊃ & Lymphocyte Mygrat⊃.
4. Stabilizes the lysosomal memb.

B. SE:

oral Cs.

- Salt & water retention & HTN.
- DM
- Disturbed fat & protein Metabolism.
- GIT irrit⊃ & Ulcerat⊃
- Activat⊃ of dormant Inf. e.g. TB, HCV, HBV.
- **Osteopenia & Osteoporosis**

IV pulsed MethylP / Prednisolone

- HTN
- MI.
- Seizures.
- Electrolyte Imbalance.
- Sudden death: ± d.t < arrythmia / pancreatitis.
- W.t gain
- Moodie change
- GIT irrit⊃
- Facial flushing.

- The S.E Can be ↓↓ by:
  - pulse #
  - Combinat⊃ #.

قاعدة مع Cs
لا تنسى ما يتبع كل دواء:
1. Prevent Pneumocystis Carinii Pn. by:
   - Dapsone or Septrin.
   - vaccinat⊃ (Pneumococcus)
2. prevent osteopenia & osteoporosis:
   - H2 Blocker
   - حموضة
   - Ca+ (1500 mg/d)

Steroid induced osteopenia

- Diagnosis: DEXA scan (Bone mineral density study).
  before # → then → Every 1 year.
- #
  - prophylactic (No renal stones): → Vit D (400-800 IU/d) + Ca+ (1500 mg/d)
  - Curative:
    - ♂: Testosterone (if level is ↓↓)
    - ♀: Est- & progest-
    - also
      - Bisphosphonate [as Allendronate]
      - Intranasal Calcitonin.

Allopurinol

A Zath. → 3 Metabolite ← Xanthine oxidase, TPMT } inactive
6 Thioguanine.

6. Thioguanine

(1). Antimetabolite — DNA & RNA
T cell & B cells.
↓ RBC & LCs

(2) Anh Ox → used in AD.

- Interaction

(1) Allopurinol → -- Xanthine oxidase → ↑ 6-thioguanine
(So ↓ AZath. level if ē : Allopurinol)

(2) ↓ level — OCPs
warfarin.

- Pregnancy D.

2nd line therapy

(Immuno Suppressives / Cytotoxic or Steriod Sparing agents)

- Include:
  - [Azathioprine
  - Mycophenolate
  - " Mofetil (MM)] → (الأهم)
  - MTX
- 3C [
  - Ciclosporin (Cyclosporine) (الاسم العلمي)
  - Cyclophosplamide.
  - Chloram bucil.

- Mechanism: [
  - Antiinflamm.
  - Immuno Suppressives.

- Indications:
  1. Failed improvement sufficient for tapering
  2. Flaring during Tapering (> 3ms)
  3. development of Cs S.E
  4. routinely used with Cs in all pts. ē Mod-severe dis. (as a Sparing Agent)

"المفروض بيظهر بعد ٤-٥ شهور او اكتر
علشان كده مش بينفع نبدأ بيهم."

1. Azathioprine (Imuran)® (50mg)

Mechanism	Dose	SE.	Monitoring
(1) Antimetabolite & Immunosupp. (↓ DNA synth) (2) Act on B cells (3) ↓ Cyclooxygenase enz. (so used in AD). Anti Metabolit / B / Cox	قبل ما تديها لازم تقيس انزيم: (المسؤول عن (Metabolism)) • thiopurine methyl Transferase level (TPMT): • NL absent in 11 % of people • high level: Aza. 2.5–5 mg/Kg/d • low level enz.: Azath. 1–3 mg/Kg/d	[BM toxicity (if ↓ TMPT) . hepatotoxicity] [Severe Nusea. . Fever] . Mg. (Leuk. & Lymphoma).	(1) thiopurine MT (قبل البدء) (2) CBC: (platelet) كل اسبوعين (3) LFTs: قبل البدء • بعد البدء بأسبوع • كل اسبوعين لمدة شهر • كل شهر لمدة ٣ شهور • كل ٣ شهور

Pregnancy (D)

2. Mycophenolate Mofetil

(Cell cept ® 250 mg 500 mg

Mechanism	Dose	SE	Monitoring
· Antimetabolite & Immuno-suppressive	1-3 gm/d or 35-45 mg/Kg/d	· GIT: Nusea & Vomiting · Hepatotoxcity & BM. toxcity: (rare) · Lymphopenia "without" Neutropenia *** (good sign ē #).	· CBC · LFTs.

· Pregnancy (D)

NB [· Very safe
[. very expensive

[· Efficacy (±)
[. Slow onset of ACT

---

3. MTX :→ · Not Commonly used (± aggravate oral lesions of PV).
· 7-20mg/w.

4. Ciclosporin:
· Mech. < -- calcineurin
-- Ig Product (through -- CD4)
↓ IL6 & IFN γ → ↓ Ig.

· Not Effective in PV or PF but effective in PNP specially those ass. with Lymphoma (or) with HL lichenoid Erupt.

5. Chlorambucil:
· rarely used.
· Considered a substitution of Endoxan (Cyclophosph.) if Hgic cystitis occurs.
· S.E: Cytopenia (unpredictable that may take months to resolve).

(HL) 6. Cyclophosphamide (Endoxan)® Cytoxan [Alkylating agent from Nitrogen Mustard family]

(Alkylating Cytotoxic).

Can be used as

Immunosuppressive "B cell > CD8 > CD4" (cell cycle independent cytotoxic)

→ 1. DNA cross-link
2. Depurinate
3. Cleaved Imidazole ring.

↓

Induces remission

- Daily oral 2-3 mg/Kg/d

والافضل ان تؤخذ مرة واحدة صباحاً وبعدها كمية ماء كبيرة جداً (٣ اكواب ماء)

to wash its Metabolite → & prevent hemorrhagic cystitis.

N.B. durable remission in 18-24 ms

. the method ↑ risk (5-10 times NL population).

Immunoablative (remove & destruct the cell population)

↓

Induces "Cure"

(but this cure remain only for 2 ys in limit its use as Immunoablative).

. Mech.: wipes all clones of cell producing antibodies.

. Indication:
- Severe resistant PV
- PNP
- SLE.

. Regimen: single, very high "ablative" dose:

. IV (200 mg/Kg) ~~daily~~ for 4 days → upon recovery from BM suppression → Cure (or prolonged remission).

الطريقة بالتفصيل:

١. يتم حجز المريض في وحدة زراعة النخاع

٢- يعطى المريض قبل العملية بمضادات حيوية (Vancomycin & Ceftazidime)

٣- IV 200 mg/Kg/d x 4 days

٤- يعطى معاه

(i) MESNA: 3 gm in ½ liter over 2 hrs / 6 hrs. (organo-sulfur compound)

(ii) Very strong Antiemetic (Zofran).

(iii) GMCSF

(iv) Erythropoietin 4000 U SC

(v) Packed platelet (if ↓↓)

- Cystitis
- Cytogenic
- Cancer
- Infect.

• S-E:

1. ↑risk of Cancer < Leukemia / Lymphoma / Cancer bladder
2. Hgic Cystitis ⟹ Cancer (if Hematuria → stop) d/t Acrolein Metabolite.
3. Sterility (♂) & Amenorrhea (♀)
4. profound BM suppression.
5. pregnancy: (D)

• Monitoring: CBC & urine analysis / week.

• NB: Cyclophosphamide is preferred as ony Neutropenia ass. with its use is predictable in onset & withdrawal of the drug ⟶ rapid recovery (in 7-10 days).

• European Guidelines (2014)

P. Vulgaris

- Mild → Cs alone.
- Severe → Cs + Immunosup. (Steroid Sparing)

• 1st line:

- Prednisone 0.5-1.5 mg/kg/d
- Taper by 25% of dose Biweekly & at < 20mg
  Taper more slowly
- Give — proton pump inh / H2 Blocker / Calcium.

• 2nd line: Azathioprine & MYCophenolate.

• 3rd line: MTX, IVIG, Cycloph., Dapsone, ...

- Other lines of Ht:

1. Nicotinamide.
2. Tetracyclines
3. Trental
4. Dapsone
5. Salazopyrine

A. Nicotinamide (& Nicotine Patch Smoke):

- Mechanism:
  1. -- Neut. & Eos. Chemotaxis.
  2. -- Histamine release.
  3. -- Lymphoblast formation & Activation
  4. ↑ Acetyl choline release & production by -- ACH esterase enz. (Cholinomimetic).

دالع س Cholinomimetic

- Dose: 0.5 gm 3 times / d.
- S.E.:
  - Headache.
  - Flushing
  - Flue like symptoms
  - Vomiting.
  - Hepatotoxicity
  - AN, pruritus
  - Icthyosiform changes.

- Uses in Dermatology:
  - Behcet
  - Aphthus ulcer
  - Acne V.
  - P.V
  - Chilblain.

Both Treat Pellagra.

(1). Nicotinic acid = Niacin = Vit B3 = Nicotinyl Alcohol.
Ros[illegible] & Rel.

- Uses
  - ↓ lipids & VD (Antihypercholest)
- S.E.: flushing

(2) Niacinamide ⇒ Nicotinamide:
- No Flushing nor ↓ lipid.
- Antiinflamm. → AV, BP.
- Topically → Bleaching

N.B: Niacin $\xrightarrow{\text{Vivo}}$ Nicotinamide

2. Tetracyclines: (2gm/day)

. Mechanism:

. Antinflammatory

. -- Neut. chemotaxis.

. -- phagocytosis

. -- cytokine product

. -- MMP. (كل حاجة)

3. Mestinon:

. Mech. → -- Choline esterase → ↑ ACH.

. Dose: 60 mg 1d.

4. Dapsone:

. Antinflammatory.

. Rx of Choice in IgA Pemphigus & P. Herpetiformis

5. Gold therapy:

. Alternative for long term Cs or Immunosupp.

. Dose — Test: 10 mg IM.

— 1w later: 25 mg IM

— then: 50 mg 1W (till) ← improvement / ↓ Ig level / Toxicity / total dose 1 gm is reached

— Maintenance: 50 mg / 2-4 ws.

~ MTX 25!

. Oral Type Called Auranofin . IM: . Thiomalate . Aurothioglucose

. S.E: . BM --.

glomerulo neph. → . GN (Immune Complex Mediated)

. Lichenoid dermatitis.

6. Trental: AntiTNF / 400 mg X3/d.

7. Tranilast:

. Mech. . Anthranilic acid derivative

. ↓ Histamine release by Mast Cells.

. Uses: . AD . PV

. ECZema . Sarcoidosis.

• Treatment of Severe / resistant PV:

- IVIG
- plasmapheresis
- Immuno-ablative
- Rituximab.
- pulse Cs

1. IVIG → see TEN
2. plasmapharesis
3. Extra corporeal photopheresis [ECP]
4. Immunoablative (ff
5. Adjuvant Immunomodulators:
   - Rituximab
   - Tacrolimus (prograf)
   - M. Mofetil
   - pulse steroid

---

① IVIG → see TEN

② plasmapheresis:

- def. the only method to wipe out all Pemphigus antibodies from circ.
- Technique: The blood is removed out of body → plasma is removed (separated) → Treated → returned to / body.
  - Treated: antibody removed. (Immuno-adsorption).

NB, in plasma Exchange: plasma is Separated → discarded → replaced by donor plasma, Albumin or Albumin + saline.

- Complications:
  - Minor:
    - Fever.
    - Chill.
    - Allergic reaction.
    - Transient Hypotension.
  - Serious:
    - Fluid imbalance (e) pulm. Edema.
      - pulm. Ed.
      - Coagulopathy
    - depletion of platelet or clotting factors → Bleeding & Inf.

Disadv.

1. Immediate ↑ in anti pemphigus antibodies ῶ are produced in extravascular compartment (false Transient ↑↑ ⟶ frequent repetition of plasmapheresis EOD).

2. Depletion of antibodies from circ. → ++ More Igs production (-ve feed back) → exacerbation of ds. in the 1st (few ds — 2ws) after 1 session

↓ avoided BY

Combined Plasmapheresis + "Pulse Cs or Endoxan" or Any other Immunosuppressives.

لازم نعطيهم ٢ غرام ٤٨ ساعة بعد الجلسة

عدد الجلسات
ليوم للبريدوم
لغاية الوصول
وتقاد.

(So) Combine pulse + plasmapheresis → the best way inducing remission.

. plasmapheresis can be used in:

- Behcet
- Wegner's granulomatosis
- Cryoglobulinemia.
- Antiphospholipid synd. (APS)

3. Extra Corporeal photopheresis:

Def: photoactivat⁻ of WBCs ē 8 Methoxsalen & UVA (PUVA) in an extra corporeal system then reintroduct⁻ of damaged WBCs → ++ clone specific immune response → down regulat⁻ of activity of pathogenic cells.

- As in plasmapheresis: should be combined ē Immuno-suppressives.

Immunoablative ##

1. Old Method → BM rescue → Eliminat⁻ or destruct⁻ of RES cells by busulphan or irradiat⁻ → reinoculat⁻ of stored BM
2. Recent Method: large dose pulsed Endoxan.

(P. foliaceous):

- Localized → Super potent C. ✓
- Generalized → ## as P.V.

(Paraneoplastic)

- Bg Tm → .. ??
- My Tm → ... ??

(IgA P.) → Dapsone (others):

- Sulfapyridine
- Etretinate / Acitretin
- PUVA
- Colchicine.

(P. Herpetiformis) → Dapsone.

الجزء الثاني
من ال Bullous

Hemidesmosome & DEJ

① Maintain the dermoepidermal adhesion in < NL Skin & Wound Healing.

② Mesenchymal-epidermal interaction.

③ Mechanical support.

④ Selective permeability & physical barrier.

. Adhesion
. Interaction
. support.

I. Structural Component

KIF = 5,14

△1 (HD) = Hemidesmosome . consists of.

Consists of < inner plaque. -> (Most cytoplasmic part that Ass. c̄ KIFs)
outer plaque. -> Ass. c̄ basal cell plasma memb.
Basal cell plasma memb. -> ملتصقة مباشرة بالخلية القاعدية
Subbasal dense plate: it is an extracellular component that lies ll to & just beneath the outer plaque & Ass. c̄ basal plasma memb.

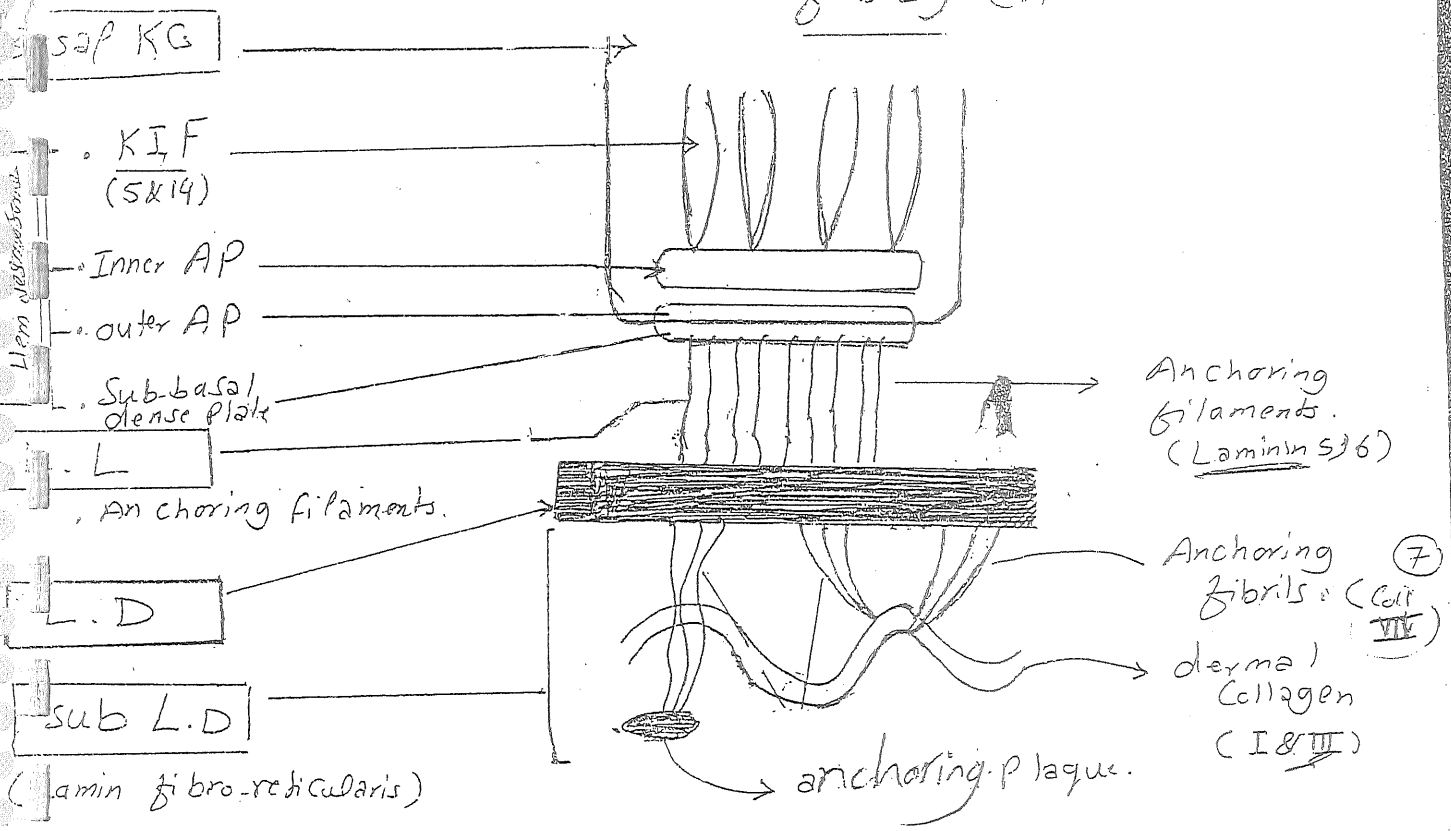
HD 3 domains
1. Cytoplasmic IAP
2. Membranous: CM
3. Extracellular domain: Subbasal d. plate.

△2 L.L (Weakest part of DEJ).
. Electron Lucent band (20-40 nm)
. Traversed by anchoring "filaments" ...
from areas underlying H.D (to) L.D
. Anchoring filaments extend from HD to LD.

△3 L.D -> . Electron dense band (30-60 nm in width)
. (E) barrier / filter that restrict passage of molecules but can be penetrated by MC & LCs.

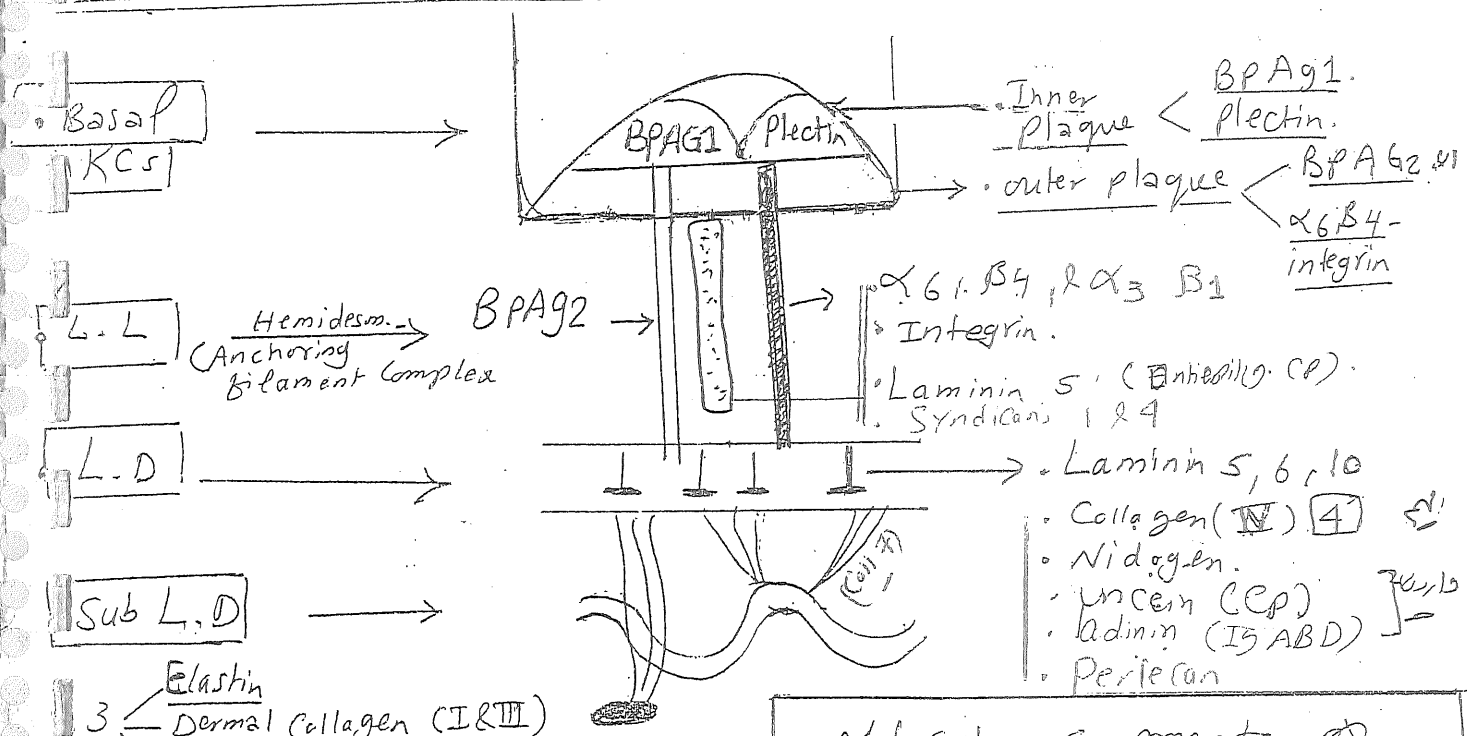
△4 . Lamina fibroreticularis = Sub LD:
Traversed by « Anchoring fibrils » that extend.
↓
Formed of Type (VII) Coll.

• Structural Components of DEJ (Hemidesmosome)



Dep: (Hemidesmosome & Basal KCs → L-L → LD → Sublamina densa).

Hemidesmosome. Anch. filament Complex.



Molecular Components of DEJ

from lower aspect of L.D &

Either ← Loop back into L.D or
insert into "Anchoring plaques" (Electron dense structures.)

Note: Anchoring ← Filaments / Fibrils / plaques.

II Molecular Component

(1) HD: (3 parts as Desmosomes)

1. Cytoskeleton: KIF → K5 & 14
2. plaque proteins: (2) [IAP]
   - BPAg1 (230KDa): attached to KIF above & BPAg2 & integrins downward. / its deficiency ↓ not harmful
   - Plectin: present in KCs & ms. Type of desmoplakin (Present in D. & HD).
3. Transmembrane protein: (2) — IAP & L.L
   - BPAg2 (180KDa)
   - Integrins (α6, β4) (its intracell. domain)

(2) L.L (Anchoring Filaments).

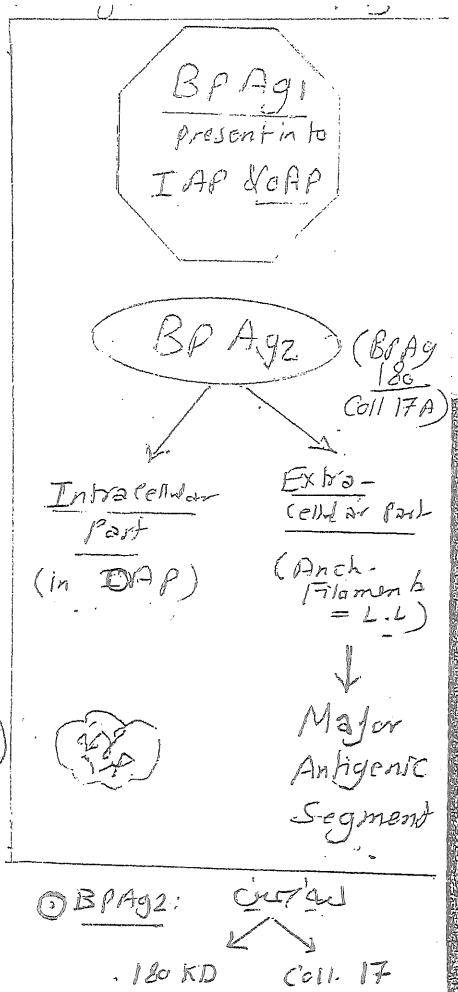
- BPAg2 (Extracellular domain)
- Integrins (α6, β4 domain).
- Laminin 5. (Epiligrin).

(3) L.D

- Collagen IV (↓ ← hematuria, RF, Eye manifs)
- Laminin 5, 6, 10
- Nidogen. (Ent)

(4) Lamina fibroreticularis (SLD).

- Dermal Collagen I & III
- Anchoring Fibrils → Collagen VII
  - Binds laminin & LD to AP.
  - ↓ Ag
- Elastin.



Subepidermal Blisters (level & Infilt.)

Basilar (separation bet L.L & cell membrane. eg basal KCs or bet L.L & Sub-basal dense plate)

1. d.t Basal cell degeneration diseases (Lichenoid dermatitis)
2. others: EBS & HG.

Intra L.L

- BP
- HG
- CP (-Ve)
- DH
- LAD (+++)
- JEB
- EBA (+)
- PCT

Sub L.D

- EBA (+++)
- BSLE
- DEB
- LAD (+)
- CP (Anti-laminin-)
- Bullous mastocytosis.

(N) Neutrophilic Infilt.
(E) Eosinophilic "
(M) Mast Cells.

Some important infiltrations

(1) Neutrophilic

- IgA Pemphigus
- EBA
- BSLE
- CP
- DH
- SCPD
- Impetigo Contagiosa
- Candida
- Pustular Ps.

(2) Eosinophilic:

- HG
- BP
- 3 Pemphigus ← Vulgaris, vegetans, PNP.

(3) Lymphocytic → Viral blisters.

(4) Scanty or Absent

- Darrier
- Grover
- H-H

- EB
- PCT
- Bullous impetigo
- SSSS
- Miliaria.

(5) Mast Cells →

Bullous mastocytosis.

(Emed 2011) Belgnia

Sub Epidermal Blistering diseases

(See : Classifical)

"Bullous pemphigoid" (B.P)

- Def → Chr., Bg, self limiting, auto immune Blistering dis. ch BY formation of Subepid blisters.
- Age > 60 Yrs.
- Sex: equally affected.
- Ass: ① Autoimmune dis. eg SLE
  ② UVB & PUVA (photo therapy)
  ③ Frusemide, ACEI. (Drugs)
  ④ Mg (Para neoplastic).
  ⑤ Neurological disorders.

لو مريض BP لازم screen for Mg. ??

Bg self limiting (5-6 Yrs)
- > 60 Yrs.
- ± ass

- C/P: Tense Blisters :-
  - usually localized to flexures. (but ± generalized)
  - on NL or Erythematous skin. (Erythem. > NL)
  - First → Empty ; then filled é cloudy fluid & ± Hgic.
  - ± Rupture → Erosions & Hyper pign.
  - (No) scarring or milia.

Skin

- - ve Signs: < Nikolsky's, Asboe Hanson.

Prodroma of B.P → ± preceded by: (Early or prodromal BP):
- Erythematous Patches
- Urticarial plaques
- Targetoid lesions.

lasting > 24 hrs → later Bullae

- Itching, moderate – Severe.

MM → Involved in about 20% (Mixed & Transient) (rare). (3e)

Clinical Varieties (13)

- Localized type:
  - Oral & Acral (Infants).
  - Vulvar (sp. girls)
  - Pretibial (Commonest site of Localized BP is Shin)
  - at sites of: irradiation, PS. or "Burns".
- Generalized: affect flexural areas or whole body.

- Bullous: (classical).
- Non B: No Bullae but: Erythematous Patches, urticarial plaques, Targetoid lesions → "prodroma"

Urticarial Stage of B.P: enter in DD if persistant urticarial lesions > 24 hrs. → as urticarial Vasculitis

- Vesicular

- P. Nodularis: (Prurigo Nodularis like but ē Blisters).
- Pemphigoid Vegetans: (Similar to Pemphigus Veget but Immunopath. of B.P).

- dyshydrosiform: (dyshidrotic Ecz. like at Palm & Soles = pompholyx).
- Erythrodermic (similar to Eryth. Ps.)

- L.P pemphigoides: (See Lip)
- Anti P 105 pemphigoid: (Severe)
  - Ag: 105 KD (Protein: in L.L)
  - CIP → acute onset. P. V (or) TEN like severe oral
  - DIF: Linear Ig G & C3.

Anti P 200 Pemphigoid.
200 KD Protein autab.
Recently Called: Anti-Laminin γ1 Pemphigoid

(37)

- Childhood B.P : ch-BY
  - Associated ē vaccination
  - Acral (Face, Hands & Feet).
  - Course < 1 Y.
- Neonatal : Acral or Generalized.

- Prognosis of B.P :
  - usually self limiting ē in (5-6 Ys). (childhood < 1 Y.)
  - some pts may die ē in (6ms - 1Y)
  - may be d.t ass. diseases.
  - MR : statistically Higher in Anti BPAg2 cases > BPAg 1.

- Pathology : (intra L.L ē Eos. infilt.)
  - Sub epid. Blisters (intra L.L) → By EM
  - No Acantholysis (Intact Epid.)
  - Eosinophils in → Blister Cavity; → upper dermis (infilt. is poly morphous ē predominant Eos.).

- DIF (Linear) : 100% → (linear) C3 ; 80% linear IgG, at L.L.

- IIF : 80% → Ig G (mainly IgG1) → Can fix Complement (Not like IgG4 of P.V)

- Targeted Ag : BPAg2 (+++) (Collagen XVII) 180kd & BpAg1 (+) 230kd.

* B.P may be ass. ē :

1. Cancer (GIT, bladder, Lung) so screening if the pt is → middle aged. → Systemic manifs are +ve.
2. autoimmune dis : SLE & IBD.
3. ass. ē : PUVA, Lichen planus & Ps.
4. Neurological disorders : MS.

Drug Induced B.P.

- Captopril (ACEI)
- Enalapril
- Frusemide
- Penicillamine

Pemph. بمفيجس
Pemphigus

- PUVA

Treatment

↓

اكتب عربي

Superpotent Topical Cs (Dermovate)

↓ Then if

Mild / Localized

dis: You Can Add

- Nothing: only Topical Cs
- Tetracyclines + Nicotinamide
- Dapsone
- Sulfonamides
- Erythromycin
- penicillin.

قاعدة

غسول الوجه: Dermovate Cream.

Control mild dis ↓ dose of systemic Cs.

أو أحسن "Tarolimus"

Severe / Generalized

dis: Add

- Systemic Cs

prednisolone 0.5-1 mg/kg/d → Controlled (usually in 2 ms) → Taper over 6-9 m.

- Other Steriod Sparing Drugs e.g. Azathioprine.

- Hard & Crunchy food: تجنب الأكل

- Chips
- raw fruits
- Vegetables.

Herpes Gestationis (HG) / (Pemphigoid Gestationis; PG)

- Why So Called that:
  - Gestationis = Pregnancy Related
  - Pemphigoid: Has — Clinical, Histological, Immuno-Pathological "Similarity to B.P"

- Incid: rare ; 1:50.000 pregnancy. , 50% during 1st pregnancy
- onset: either during pregnancy: usually 2nd or 3rd (75%) Trimester.
  - or Postpartum:
    - (i) early → late preg. → Recur Postpart.
    - (ii) 2nd or 3rd
    - (iii) Postpartum
  - (may occur or Exacerbate) (25%) = → (75%)
- Recurrence: with Subsequent pregnancy
  - also: OCPs (25%)
    - menses
    - postpartum
    - VM or Choriocarcinoma.
- Course: resolut ± late pregnancy → Flare → Spont Resolut (6mo)
- Complications: (rare)% (Fetal or Maternal)
  - Prematurity
  - HG ∑ fetus (3-10%; mild & self limiting).
  - ↑ MR.
  - BP

- Risk of malignancy of Course
  1. ↑ Age
  2. pseudolymphocytic
  3. Mucosal ++

- CIP: Itchy. Severely Erythematous papules & plaques at abdomen (Specially periumbilical) → spread to involve Trunk back, buttocks & arms (2-4 wk) → Large, Tense bullae ± in annular config.
- NB:
  - Sparing: Face, scalp, palms & Soles & MM (20%) (Acne+MM)
  - Some Cases: no Blisters, only Erythem. plaques

- Path. → as B.p
- DIF: → 100% linear C_3 (at L.L)
  → 40% IgG
  → salt split skin: → Epid. side Fluorsc.

- IIF: (25%) → "HG Factor" (Circulating IgG1 that binds To BpAg2 (+++) & BpAg1 (+))

- Pathogenesis: "مهم"

AbNL expression of MHC II at chorionic villi (of paternal haplotype origin) (HLA DR3,4, DP, DQ) → IR initiation against placental BMZ Ag (called HG Ag) (Immune Response) (Anti HLA Abs) → autoantibody production (IgG1) (Called HG Factor) That Cross React with skin BpAg2 → HG

- Treatment: (براً ليس)
  - Backbone: Cs (systemic) "الأهم"
  - others: (Emed 2010):

Cs & pregnancy (C) — (Category C)
1st Trimester
Cleft Palate
others.
placental calcification
LBW.

- Other lines:
  - Emollients, Tepid baths & Compresses.
  - Dapsone
  - Nicotinamide + Tetracycline (ممنوع في الحمل)
  - plasma-pharesis
  - IVIG.

- mild dis. → Topical Dermovale + Antihistaminic
- Severe → Cs.

· (2011) · Bologna

Cicatricial pemphigoid (CP) (Mucous memb. Pemphigoid)

- Age: 62-66 y.
- Sex: M > F = 1:2
- Remission: less incid < B.P

هو اصابة الـ MM وتعلمه في قلة من الحالات يمس الجلد (25%)

chr. blistering dis. affects:

· Mainly MM

Gingiva > palate > buccal (most common)
Mouth (100%)
→ desquamative gingivitis & Erosions → Scarring (Reticulated L.P like)
(cotton tip & Blowing → peeling of Mucosa)

other MM: Nasopharynx, oesophagus, Genitalia. (LSA like of vulva)

- Supraglottic → obst. → Tracheostomy.
- Healing of oral: reticulate like L.P.

Eye (80%) [ادخل عليها]
① Chr. conjunctivitis & vesiculation → Corneal ulcer & scarring.
② Synechia
③ Ankyloblepharon
④ Entropion & Trichiasis.

· occasionally (25%) Skin → 3 Varieties

· Localized (commonest)
Erythematous plaque(s) ē Tense Bullae & Vesicles (± Hgic):
at: scalp, Face, Neck, Trunk
ŵ are the sites of Recurrent Blistering
↓
Severe atrophic scarring

· Generalized (less common)
Generalized disseminated lesions Resemble (B.P)
↓
± SLD

· Brunsting-Perry pemphigoid
· Elderly ♂ affect the head & Neck without MM (Later → MM)

(أزرق) Mucosal oral Biopsy

· Pathology: Intra L.L Blistering ē mixed infilt. or no infilt. [Oral → plasma cells] — cell-poor
· DIF: 80% Linear IgG & C3 (at) DEJ.
· IIF: 20-30% IgG1 (Low titer).
· Targeted antigen: Laminin < 5, 6] "anti-laminin CP" (Antiepiligrin) → SLD separate
- BP Ag < 1, 2 (+++)
- α6, β4 (integrin) → ocular CP

Commonest BP Ag2 & Laminin 5

- NB . BPAg2 : most Common Targeted Ag & (موجود)
→ +ve salt split skin Technique at epid. side.

Laminin 5/6 (Anti Laminin CP) (Laminin 332)
(٤ مرضى قصص)
+ve salt split skin Technique at the dermal side.
ch. By
(Mg associated) (Adenocarcinoma)

Sal split skin Tech. & CP
→ Epid side: most cases → Anti BPAg2
→ Dermal side: some cases → anti laminin CP

Treatment

1- Mild dis (localized) (oral / Cut) → as BP → (Cs < Topical / IL + Tetracycline oral wash)
→ Dapsone (1st line) or "Sulphapyridine"

2- Severe dis: ocular, Laryngeal, pharyngeal, Esophageal, resistant oral or skin to Topical IL
↓
Cs + Cyclophosphamide

NB: (1) CP Sparser < Infilt. by HP (cell poor) / Immunoreactants
· DIF: 80%
· IIF: 30%

(2) Most Common Ags: "BPAg2 & Laminin 5".
α6, β4 → ocular CP.

(3) Cell-poor Bullous dis:
- BP
- EBA
- LAD
- PCT

(4) DD of Chr. Severe / Persistent oral erosion < PV, PNP, CP, LP ± SJS / TEN / EM.

DH (Dermatitis Herpetiformis) 45

(Duhring dis)

Def
- very chr (life long)
- Relapsing
- autoimm.
- vesicular dis

⟹ "Considered as Cut. manif. of Gluten sensitivity"

- Age → dis. of all ages (20–40 y)
- M > F (2:1)
- HLA < B8, A1 / DR3, DQ8
- Ass.
  - Common:
    1. GSE → 90% Asymt. ass. c̄ Mucosal atrophy & Intest. Lymphoma
    2. DM (Dermatoses)
    3. Hashimoto's Thyroiditis (25%)
  - Rare:
    4. Mg. (Lymphoma) (Enteropathy ass. T cell lymph).
    5. CAH.
    6. M.G.
    7. L.E.
    8. Diabetes.

x Clinically (No oral affection) — +ve oral but Asympt.

Adulthood DH

Eruption
- Polymorphic: < papules, vesicles < Bullae, urticarial or Targetoid lesions.
- grouping
- Bilat., Symm. on extensors:
  - of limbs.
  - shoulders.
  - buttocks.
  - Postaxillary Folds.
- Severely itchy (paroxysmal)
- Healing: scarring & pigm.

Flaring: usually c̄ ingestion of Gluten or Iodide containing food"

Abdom. manifs: pain or diarrhea, undernourishment.

Childhood DH

↓

as in adults + Palmar blisters or Brown macules.

NB: the clinic finding is spont. Remission that lasting as long as 1 w that terminating abruptly c̄ New Crops.

Pathogenesis of DH

- Pts with: Gluten sensitivity = Defective Mucosal barrier

- Gluten: Containing diet e.g Wheats → Passes to lamina propria of The Intestine.

- Gliadin: is frachim of Gluten
- TG2: enzymes Tissues (TG2) use Gliadin as substrates

↓

Gliadin-TG2 Complex

↓

Formation of (Anti-TG2 IgA autoantibodies)

↓

Cross react with Epidermal TG3

↓

Formation of IgA-TG3 Immun-Complexes

↓

deposition in dermal Papillae (with Neutrophil chemotaxis.

- Subepid. blisters (L.L)
- Neutrophil Microabscesses of (IgA → ++ C3a → ++ Neut.).
- granular Ig A deposits at dermal Papillae.

- Dapsone: -- Neutrophil accumulation
- Iodides: ++ " "

Dapsone is ## of dis. of Neutrophils or IgA.

((NB))

يعني
نبتديه دابسون
و GFD ثم توقف
الدابسون ونكمل
GFD

- **GFD** = Gluten - free diet

لحد ما نحصل ٦ شهور
Dapsone نقلل ثم بنبتدي ع ٢ أشهر

- **Sulfasalazine:** Category (B) in pregnancy.

  - **Dose** : 1 - 2 gm/d
  - **Sulfapyridine** : 0.5 - 1.5 gm/d.

- **S.E** . Hypersensitivity
  - Hemolytic anemia
  - Proteinuria
  - Nausea & Vomiting الأهم

لازم يشرب كتير مادة لبنية

- **Sulphapyridines:**
  - Sulphasalazine
  - Sulphapyridine 1.5 - 4 gm.
  - Sulfamethoxypyridazine 0.5 - 1 gm/d

- Path: → subepid (intra L.L) blisters ē Neutrophilic infilt.
  → Neutrophil microabscesses (in) dermal papillae.

(تصاحبية) Intact bulla or Erythema

Eos. infilt is +ve so difficult to diff from BP.?? ↓ do (DIF)

أهم حاجة للتشخيص . DIF: → . 90 % (granular) IgA in Papillary dermis. [hallmark] "مهم جداً"

(HL) . NB : Granular + linear (5-10%) . Fibrillar : rare.

. IIF: Anti (IgA) — . gliadin
. TG (Transglutaminase) [antiendomysial]
. Reticulin

. Targeted Ag : → Transglutaminase → Tissue : TG2 → Epid = TG3

---

(44)

ممنوع أكل:
- bread
- Cakes
- Salad,
- Alcoholic beverages.

[Stop gluten] (Atkin diet)

- كُل : O R C (oats الشوفان, Rice, Corn ذرة شامية)
- لا تأكل : Wheat القمح, & Rye الجاودار
- Value :
  1. ↓ Cut & intest. manif.
  2. ↓ Dapsone or (Stop it)
  3. ↓ incid of Lymphoma.

↓ give

[Dapsone or sulfapyridine]

Dapsone (ردة فعل / علاج تشخيصي):
1. 100-200 mg/d (± ↑ upto 400/day لكن تدريجياً "Hemolysis")
2. dramatic Response ē in 48 hrs. (استخدامها Therapeutic Test)
3. For 3-6 ms.

Sulfapyridine:
. 2-4 gm/d
. sulfasalazine 1.5-4 gm/d عكس → metabolized To → sulfapyridine.

[طب لو مفيش دابسون و sulfapy.] → Colchicine, Tetracycline, Nicotinamide, Ciclosporin (but ↑ intest. Lymphoma), Heparin زي ما هو

Cs → Systemic : No effect
→ Topical : ± ↓ itching

LAD = linear IgA Dermatosis

(LABD = linear IgA Bullous D)

1- Classical lesions: Clear & Tense Hgic roundish or oval vesicles & bullae on NL or Erythematous or urticarial skin

- Itchy
- Vesicles < Clear & Hgic
- Skin < NL / Erythe. / Urticaria
- MM ← 50% ← Severe + early
- Distribution
- Types of LAD
- Variants

These vesicles & Bullae maybe arranged into 3 varieties.

- discrete (CBP like)
- Grouped (Herpetiform) (DH like)
- at Edge of annular or Poly cyclic Erythematous or urticarial lesions. ✓ → String of pearls or Beads sign

LAD & DH يوجد تشابه بين

2- distribution & lesions

Adulthood LAD (≥ 52 Y)

- Usually → Trunk & Limbs (→ lower)
- Rare → perineum & perioral

Childhood LAD (CBDC)

- start 5 Y
- Resolve: 13 Y (after 3-6 Y)
- Usually → lower Abd. Anogenital & perineum
- Others Face, perioral, Hands & Feet. (Acral)

2- other Non classical lesions:

- Erythematous ← Macules, papules, plaques
- EM-like (Targetoid)
- Morbilliform
- Cicatricial Variant: EBA or CP like (severe Mucosal effect)

LAD عند الأطفال

LAD in children called chronic Bullous dis. of childhood (CBDC)

- NB: Skin lesions are itchy & have Burning sensation (but < DH).

MM affect (≃50%)
- Comm & ± Early sign.
- has Cp like picture. (severe)
- Any Mucosal site ± affected.

- Pathology:
  - Early urticarial lesions:
    - linear alignement of Neut. at BMZ.
    - Neut. Microabscesses at dermal papillae (DH like).
    - Vacular changes.
  - Late / vesicular lesions: intra L.L & ± SLD
    Blistering ± Neut. infilt. (± Eos.)

- Path res & DIF

DH:
- granular IgA & Neut. at dermal papillae

LAD: linear IgA & Neut at very tip.

- NB
  - Path → Non Specific (BP ≠ DH like)
  - But linear arrangement of Neut. along BMZ & Neut. at the (very tips) of dermal Papillae → Favors LABD > DH.

- DIF:
  - Linear IgA at
    - L.L (Mainly)
    - SLD (as. ē Anchorin fibrils) (±)
  - ± linear C3 & IgG

- IIF: ≃ 50% IgA antibodies directed against:

(Ag)
- i.L ≤
- LD -
- SLD -

- L.L antigens: or
  - 97 KD
  - 120 KD [Portions of Extra-Cellular domain of BPAg2]
  - 285 KD [Ag in L.L] (LAD 285)
- SLD antigen:
  - Anti Coll 7 antibs. (Anti-250 KD protein Abs ≠ to part from Coll 7A).
- Other Ags:
  - Laminin (in LD has role in Maint. of Forma of Anch. Fibrils)
  - BPAg1

NB1: Conditions that may associate LABD:

- ulcerative Colitis (70%)
- Malignancy
- Drugs.
- Gluten sensitivity (GSE). (Rare)

NB2. Types of LABD: 4 Main types:

1. Idiopathic (Classical) Type: 2 Age peaks
   - preschool (5y)
   - 60 ys.

2. Drug induced: (جدول برلدنيا)
   - Most Common: Vancomycin (مهم جداً)
   - less Common: ACEI, NSAIDs, penicillin & Cephalosporins, "diclofenac"
   - uncommon: phenytoin & Sulfa.
   - rare: Ciclosporin, PUVA, Rifamp.

   2 Ch:
   - No MM
   - resolve after stop of drugs.

3. Malignant associated.

4. GIT disorders ass: GSE & U. Colitis.

- Prognosis of LABD: in Majority of cases; resolve after 3-6 ys.

  (نسبة الشفاء: 10-15% in / 30-60%)

Treatment

أهم علاجهم

1. Dapsone: (الأهم) → dramatic c in 2-3 ds.
   - children: 1 mg/kg/d
   - Adult: 100-150 mg/d.
2. Sulphapyridine: (بديل للدابسون)
   - 250 mg – 1.5 gm.

- Others:
  1. CS (systemic) — ممكن نحتاج نضيفها للدابسون علشان نغطي سيطرة أفضل.
     - Usually Needed for pt. c IgA & IgG deposit.
  2. Others (مهم): Tetracycline, dicloxacillin & Erythromycin
     - other Immunosupp.

EBA (Epidermolysis Bullosa Acquisita) (4-1)

- 40-50 Ass.
- خاص ذاتي

HLOR2

- Age: Any but more in elderly (40-50)
- M > F
- Ass.
  - DM (dermatomyositis)
  - SLE
  - lymphoma
  - Myeloma
  - Amyloidosis
  - IBD

HLCTD
MG
IBD

Clinically

Generalized Inflamm. type (non-scarring) → B.P (Dermolytic P.) or CP like.

- CP → wide spread tense bullae → No scarring
- (HI) (good prog. / responsive)
  1. Cs
  2. Dapsone
  3. Immunosupp.
  4. IVIG

Localized non inflammatory type (commonest) → DEB or PCT like [So called Acquired Mechanobullous]

- PCT → Skin: Traumatic blistering (Fragility) scar, Hyperpigm. & Milia. (Acral & Trauma Sites: elbows, knees, dorsal Hand & feet.)
- Hair → scarring Alopecia.
- Nail → dystrophy
- MM → usually affected. (HI) [prolonged / resistant to HI]
  1. avoid Trauma
  2. wound manag.m
  3. # inf

Path.

- Histopath: Subepid (Sub LD) or ± L.L Blisters
  - Neutrophil → inflamm. type
  - non inflamm. type → Absent (or) sparse infilt.
- DIF (100%): Gold standard B.P → linear IgG (±IT) > & C3 (+) (SLD) diagnostic
- IIF (50%)
  - Anti BMZ Abs directed against Collag. 7 & 8 Anchoring Fibrils in Sub. LD (IgG only)

Supply DD < BSLE BP

of EBA

(very chr. dis & very resistant to ##)

- No universally accepted ## d.t lack of studies & rare cases.

- Best ## by some authors:
  - Steroid + Dapsone or Sulphonamides.
  - Colchicine
- Other lines:
  - Pulse Cs
  - AZath.
  - MTX
  - Vit. E & C
  - Ciclosporin
  - IVIG
  - Plasmapheresis

Bullous SLE

- IgG & IgA against Coll 7
- during exacerbation (SLE)

- Def. Transient autoimmune blistering condition that occurs in the setting of SLE (1% of cases)
- NB: there is some controversy as to whether the term include all bullous erupt° in SLE or should be reserved for those w/ derma Ag. [Coll 7].
- CIP / Typs / Criteria for Dx (see CTDs)
- Histopathology "Lever" 3 Histologic pattern:

Subepid. Blistering w/ dermal Neut. Microabscesses

1. DH like → Most Common.
2. Basal cell layer vacuolization & subsequent blistering
3. Vasculitis w/ subepid blister & pustule formation.

(to diff. from DH: . Mucin deposit (among Collagen)
. Thickening of BMZ.

BSLE

1. ~~DIF~~
2. CIP → B.P or (DH) like Sp. at sunexposed + SLE picture
3. Pathology, DIF & IIF → as EBA

"Generalized Sp. at sunexposed"

(4) Steriod., Dapsone, MTX or Rituximab.

(Nicola) So How to diff.

- EBA
  - Trauma site
  - Skin fragility
  - Heal e scarr.
  - IgG only

- BSLE
  - sunexposed areas (mainly)
  - Hx & manif ≈ SLE
  - dramatic Resp. (+) dapsone
  - IgG & IgA.

2 diseases dramatic Response to Dapsone ?? → DH & BSLE (also LAD)

EBA & B.P

- Blister → B.P: L.L. / EBA: SLD.
- infilt → Eosin. / Neut.
- C3 → : B.P > IgG (which) EBA
- Salt split skin
  - BP: epid. side.
  - EBA: derm side
- Skin Biopsy & Immunohistoch
  - Collagen 7 Abs < BP: at base of bliste / EBA: " Roof. "
- DIF: EBA → U serrated pattern / BP linear.

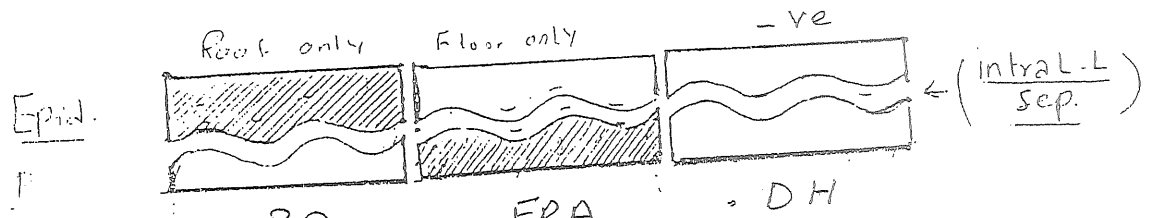
- EBA & BSLE → clinic
- BSLE → clinically as → DH or B.P
  Immunologically → EBA.

Salt split skin technique.

Subepid. اختبار واحد لكل

separation of DEJ through (L.L) by osmotic.. exposure to hypertonic 1 molar NaCl for 1-2 days at 4°C, (is) essential for IF evaluation of subepid bullous dis.

. Can be done for both DIF & IIF., the later the auto Abs will react the epid. or dermal side of skin.



- BP
- CP
- HG
- LABD (Majority)

(anti BP Ag2)

- EBA
- BSLE
- BP (anti-P 105 ✍)
- CP (anti laminin CP)
- LABD (minority)

Dapsone in Subepid. Blistering dis.

- localized CP
- DH
- LABD
- EBA
- BSLE
- SCPD

Non Auto Immune Bullous diseases

Subcorneal pustular dermatosis (Sneddon & Wilkinson, 1956)

It is a chronic benign relapsing pustular eruption which affects mainly the trunk, spares the face and mucous membranes and histologically shows subcorneal bulla which contains polymorphonuclear leukocytes.

- **Age:** 40 - 50 ys., **Sex:** more in female (4:1).
- **Clinically:** Chronic relapsing disorder, with sterile pustules in annular or serpiginous patterns mainly on the abdomen, axillae, and groins. Pus accumulates in the lower half of large pustule (level). Healing occurs with superficial crust and later on with brown pigmentation. The face is never affected nor the mucous membranes.
- **Associations:** IgA monoclonal gammopathy, pyoderma gangrenosum, inf. bowel dis.
- **Histopathologically:** Subcorneal neutrophils. Later, few 2ry acantholytic cells are seen at the base of a pustule (probably due to proteolytic enzymes present in the pustular content). Dilated capillaries and perivascular mainly neutrophilic infiltrate are present in the underlying dermis.

  Some authors believe that subcorneal pustular dermatosis is a variant of pustular psoriasis, however, spongiform pustules occur only in pustular psoriasis.
- **Treatment:** Dapsone 50-150 mg daily or sulfapyridine.

Subcorneal or intracorneal separation with:

Neutrophils predominant	Eosinophils predominant	No or few inflammatory cells
• Impetigo contagiosa	• Erythema toxicum neonatorum	• SSS syndrome
• Pustular psoriasis		• Bullous impetigo
• Subcorneal pust. dermatosis		• Pemphigus fol.
• IgA pemphigus (SPD type)		• Pemphigus erythem.
• Candidiasis	• Eosinoph. pust. folliculitis	• Miliaria crystallina

- IF → -ve but recently IC IgA in epid.

- NB:

SCPD like dis

- pustular PS.
- SCPD like IgA Pemphigus.
- Amicrobial pustulosis of the folds
- Pyoderma Vegetans.

(1939) اكتشف · Hailey - Hailey (By Familial ch. pemphigus)
(Darier أخوال)

(EMed 2dk) Darier

· Inheritance
  · AD
  · + FH → (60%)
· Age: 30-40 ys.
· Pathophysiology: Genetic + others

[· ATP2C1 / hSPCA1 → desmosomal defect → Blistery.

(Ca+ Pump Protein)

· defect on gene called (ATP2C1) Found on (Golgi)
  Chromosome 3q21-24 Codes For protein hSPCA1 (PMR-1)
  ω is Ca+ & Mn. pump → defective desmosomes (depend on Ca+) → separate

Key Darier

· Other Factors Share in the dis.:
  · Heat, Frict., Inf (Bact & yeast)
  · UVB: provoke acantholysis (& used to detect Gene Carriers of the dis.)

· ultrastructural studies: KCs show:
  · retracted tonofilaments
  · Elongated memb. microvilli
  · ↓ No of desmosomes.

· C/P: → Flaccid Vesiculopustules: < crusted lesions. / circinate ". / vegetating ".
  · that rupture → Crusted lesions or
  · form expanding Circinate plaques ē central healing → Pigmentation or
  · Form moist, Malodorous flat soft Vegetating ē painful Fissures & (2ry Inf.)

Site → Flexures (one site or Multiple sites)

· Pain, burning & itching → limit the mobility of Flexures.
· other ass. cut. lesions: < PP pits, white nail bands, Mucosal: rare oral (buccal) ± Vaginal or Esoph. → Darier.

· Complication: 1- Eczema Herpeticum (عام)
2. ACD
3. Malignant transformation → SCC (نادر)

· prognosis:
Exacerbat^ usually at warm seasons.
improvement ± occur in old ages.

· Pathology: حاجتين مهمين ← Dyskeratosis (±), Acantholysis: (+++):
↓
(Early)
· dissolut^ of: APs
· Tonofilament Separat^ → aggreg. around NUC. → Dyskeratosis

→ Suprabasal Acantholysis (widespread)
· Extensive but < PV
→ Few bridges (desmosomes) remains → Dilapidated brickwall

→ Villi inside the Blister Cavity.
(Elongated dermal papillae) & a single layer of Basal Cells lines the villi.

· ultrastructure: → (as) before"

· IF: → ??

· Treatment [Course Waxes & wanes].

1. Topical: (Astringent Agent).
· Soothing Compresses: Alum. Acetate (1:40) dilute, Alum. chl. 20% in Alcohol
· Topical Cs
· Topical Antib. & Antifungals.
· Diavonex (Control Ca+).

2. Systemic:
· Antibiotics (tetracycline & Erythromycin) → ↓ protease Activat^
· Cs (↓ Acantholysis).
· MTX
· Retinoids (Few reports) +ve Emed.
· PUVA (±)

3. Recent
· Botox → ↓ hyperhidrosis.

4. Grenz Zone Therapy.

5. Surgical: dermabrasion + CO_2 laser, Cryo

(EMed 2009)

Acantholytic Dermatosis (AD)

- Transient AD (TAD → Grover's dis (1970)
- Persistent AD (PAD → 1976).

often persistent & resistant to tt so the PAD

- Age: ♂ > 50 Ys.
- Exacerbat: Summer, Sweating, Sun light, Heat & Fever
- lesion: discrete papules or papulovesicles.
- Site: central back & chest, neck, lower part of rib cage
- Itching (...chic)
- Course: Transient: ws - ms; persistent: several (Ys).
- Ass. [AD, CD. — X. Eczema, Cancer skin.

Aphthae like oral lesions (±) occurs.

- Pathogenesis:
  - small molecules seep through sweat → Acantholysis
  - mild thermal injury → enzymes → Acantholysis
  - M. Furfur
  - Demodex
- Histopath.: 5 Histological patterns:-
  - PV like.
  - PF like.
  - Darrier like.
  - HH like.
  - spongiotic dermatitis like.

Focal Acantholysis + Dyskeratosis + Spongiosis

- IF → -Ve (as non Immune Bullous)

- Topical: Potent Cs, Menthol 1st
- Systemic: VitA, Isotretinoin, Cs. PUVA; MTX

OK.

• EBS (Epidermolytic = Intraepid Blistering)

(الحويصلات الماء)

1. All AD Except < Muscular dystrophy Type (AR). / Some Cases of Koebner (AR)

2. All dating since birth or Infancy Except Weber-Cockayne.

3. All d.t defect of K5 & K14 (KIF) Except: (Plectin, Integrin)
   - Muscular dyst. → (Plectin)
   - Mottled Pigm. Type → K5 only
   - AR Koebner Type → K14
   - ✗. EBS Superficialis → Coll. 7 ?? & plectin.
   - ✗. Ogna & Pyloric Atresia → (Integrins) ??

4. All without → scarring, milia, MM, Nails, Teeth & hair
   Except → Dowling (Scar, milia, MM, nail) & Musc. dystrophy (MS).

Other Rare EBS:
1. EBS Superficialis
2. lethal Acantholytic
3. Plakophilin 1 deficient
4. AR

• Types (WKODW)

• W → Weber-Cockayne (localized Type)
  - Palmoplantar only
  - at Childhood.
  - طفل أو شاب بيجيله باستمرار فقاقيع مع المجهود والمشي الكتير

• K → Koebner (Generalized)
  - AD ≫ AR
  - Generalized (SP) at large joints. in Infant & child: occiput, back, Leg & large joints, also pp.

• O → Ogna (Bruising)
  - Hgic bullae
  - Easy Bruising
  - Nail onychogryphosis.
  - (بسبب) ↓ RBCs enz Glutamic Pyruvic Transaminase).

• D → Dowling-Meara ("Herpetiform")
  - grouped (or) Herpetiform in Polycyclic or Annular pattern.
  - PPK
  - Scar, Milia, Mucosal & Nail aff.

• W with < Mottled Pigm. / Musc. dystrophy

• Most Common Types: • Weber • Koebner • Dowling	• Most Severe: Dowling (Herpetiform)

JEB (Atrophic EB)

(Blistering at Level of L.L).

Sheet

1. All AR dating since birth.
2. All d.t defect in Laminin 5 → Genes: LAMA3, LAMB3, LAMC2
   - Except:
     - GABEB → BpAg2 (± laminin 5)
     - JEB ē pyloric atresia → α 6, B4 integrin.
3. All show:
   - Atrophy & scar.
   - Hair
   - Nail
   - MM
   - Teeth (dysplasia) مهم

   + (Except) "Gravis" minimal scarring & milia.

مهم → Atrophy; Teeth dysp (Enamel) لكل الأنواع (pitted teeth)

الانواع:

- Herlitz (lethal) — 2 ... Extract.
  - ↓ أول ماتتوقع ... مولود → "Ensure Air way"
- Non Herlitz (non lethal) — باقي الأنواع
  - mitis
  - NH-PA
  - GABEB
  - localized
  - cic.

Most Common:
- Herlitz
- GABEB

A. Gravis (Herlitz = Lethal)

1. Systemic & Mucosal affect:
   - anemia
   - GR
   - GIT affect
   - Corneal affect
   - laryngeal " → Hoarseness → Omnious sign at birth

2. Cut. Manifs: Generalized blistering ē Marked Facial Erosions & chic peri oral, peri-nasal & perianal Exuberant G.T.

   أول شهرين → RD, Death (Elect. imb. & inf.)

2. No (مش بيعمل لا تغيرات):
   - Hand affect.
   - Scarring (بيعمل ثانياً بيموت)
   - milia.

B. Mitis

as Gavis Except:
- No systemic
- No GT.
- Non Fetal (Good prognosis)

C. With pyloric Atresia

ass ē ...

D. GABEB

as Herlitz except:
- Atrophy (no scarring) → الاسم الجديد Non Herlitz
- Non Fatal
- Bald, Atrophic scalp
- ± SCC.

(E) Inversa: Flexures (30)

(F) Cicatricial: Scarring → Syndactyly & ant. Nasal Stricture

(G) Late onset: at PP, Elbow, Knee
: Deafness & loss of Finger print.

(H) LOC synd

DEB (Dermolytic) — d.t defective Collagen 7

(Separation at level of SLD)

AR (RDEB) = Hallopeau S. / Others:

- 4 Ch: Poor prognosis. More Severe. Acral deformity. Extracut. manifs.
- Others: mild Generalized, Inversa, Prurigihasa, Centripetalis, BDN (ARIAD).

AD (DDEB)

- 4 Ch: good prog. less severe. No Acral deformity. No Extrac.

NB: RDEB: Hallopeau Siemens (HS) [Mutilating] / Non H-S: mixed non mutilating Type, Inverse, Centripetalis.

- 6 Types:
  - Generalized
  - Acral
  - pretibial
  - Prurigmosa
  - BDN
  - Nails only.

① Hallopeau Siemens (Gravis)

(Skin + systemic)

- Generalized scarring
  - theres: Milia, Alopecia, M/M, Nail, Teeth (Severe dental caries)
- Anemia, GR → Clubbing: club like Feet or mitten like deformity (occ. at 25 y)
- Oesoph. stricture
- Systemic Amyloidosis (Fatal)
- ↑ Risk of SCC (esp)
- Osteoporosis

(Pseudo Syndactyly: Fusion bet Fingers & digits → resorption of bone & muscle. Atrophy)

(Non H-S RDEB)

- Mild Generalized: less severe than H-S
- Inversa: at Flexures
- Centripetalis: Slow progressing from Acral → Trunk.

· AD DEB (DDEB)

1. Cockayne-Touraine

3 ⎧ 2. Pasini
   ⎪ 3. Pretibial DEB
   ⎩ 4. EB Pruriginosa (AD > AR)

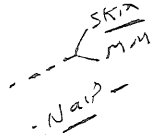
(Transient) (TBDN) → 5. Barts Synd
                     6. Bullous dermolysis of the new born (AD/AR)

---

1. Cockyne-Touraine [Classical DEB]:

Sharp Knock → Skin + Nail + MM

. less Cut. Fragility than RDEB → Sharp (Knocks) or Blows are need to induce bullae rather than mild Fric□.



. Skin: Acral blistering (Elbows, Knee, dorsal Hand & feet) → localized scarring & Milia.

. MM → NL ē NL Teeth. (Atrophic or Hyper□)

. Nails: dystrophic (very chic as many Pt has mild scarring)

2. Pasini = Albopapuloid: as Cockayne but:

. More Severe (± ē Nikolsky's sign).

. Albopapuloid scars: Spontaneous, Flesh Colored, Ivory White perifollicular scar like papular lesions on Trunk (sp. Lumbosacral).

3. Pretibial DEB: itching, bullae, Atrophy & Scarring at Shin.

(4.) EB pruriginosa:

- Severe itching
- Mild Acral Blistering
- linear, Victareous papular & Nodular lesions at shins & forearm.
- Nail dystrophy

(5.) Barts Synd.:

- Skin Fragility ≤ + "Cong. localized Absence of Skin at lower legs."
- Ass. Features: Cong. L.L Anomalies, Renal Aplasia & Mandibulofacial distasis.

(4.) Bullous Dermolysis of ! New.born (Transient BDN)

vesicular ullous Eruption at birth that's induced by Friction resolves spont. at 4 ms without scarring.

Mixed EB = Kindler synd [AR].
(Acrokeratotic poikiloderma)

- Generalized Poikiloderma
- Photosensitivity
- Acral Blisters. (PD)
- Acral Keratoses
- Pseudoainhum.
- Gingival Affection

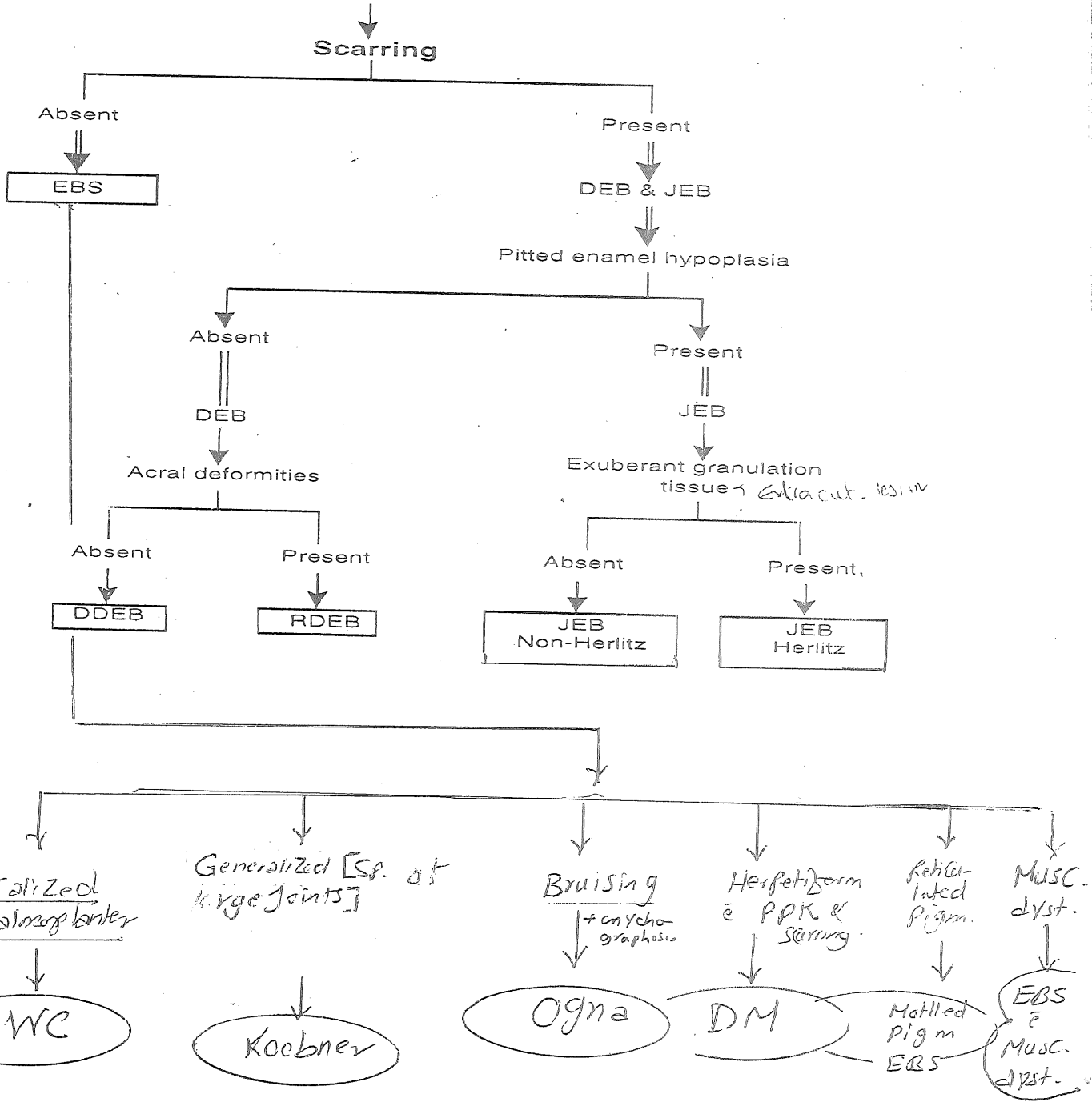
Diagnosis of EB

A. Clinical : Hx & Exam

B. Lab. - Biopsy
- Ag Mapping
- Antibody using [Immuno-histochemistry]
- Molecular diagnosis.

A. Clinical Diagnosis

Family history and examination



(WKODW)

Lab. Diagnosis

(33)

1. Skin Biopsy: to determine level of Blistering.

2. Transmission E/M:

determines 2

- Blister level
  - EBS → Basilar (Intraepid.) ↓ Just above HD & CM.
  - JEB → Intra L.L
  - DEB → SLD
  - EBSS → Subcorneal.
- Evaluation of Basal KCs
  - Tonofilaments, HD & Fibrils

EB subtype	Ultrastructural findings (Pathognomonic)
EBS	Clumped tonofilaments in EBS "Dowling-Meara" (NL WB)
JEB	Absence or markedly reduced numbers of hemidesmosomes
DDEB	Reduced number of anchoring fibrils
RDEB	Absent or markedly reduced numbers of anchoring fibrils

3. Antigen mapping:

. Immuno histo chemical staining of DEJ

By using Antibodies against:

- K5 & 14 → stain Basal KCs (Basal KC ↓)
- BPAg1 (320 KD) → stain lower surface of ↓
- Laminin 1 → stain LL & SLD
- Type VII Collagen → SLD

Split-Skin Test

Fluorescent labelled Abs: [Blister للبلاعيم]

- EBS: all Abs stain Base (Floor) of Blister Except Anti K5 & 14 stain the roof & Floor
- JEB
  - Anti Keratin & Anti BPAg1 → Roof
  - Anti Coll 7 → Floor
  - Anti laminin 1 → roof & Floor.
- DEB All Abs Stain Roof only.

(34)

4 Immunohisto Chemistry; For detection of ↓ or Absent Ag. Expression:

By using monoclonal Abs → ↓↓ staining of Targeted Antigens in Each Type of EB (اذكرهم ...)

Abs: < 19 DEJ-1 → -ve staining in all JEB; LH7.2 → " " RDEB.

Mutational Analysis (تشخيص) AR

5 Molecular Diagn:

6 Collagenase: → ↑↑ in RDEB

↓ ↑ degradation of Coll < I, III, VII

Treatment < No specific therapy; No Effective "; Based only on avoidance of Trauma Friction

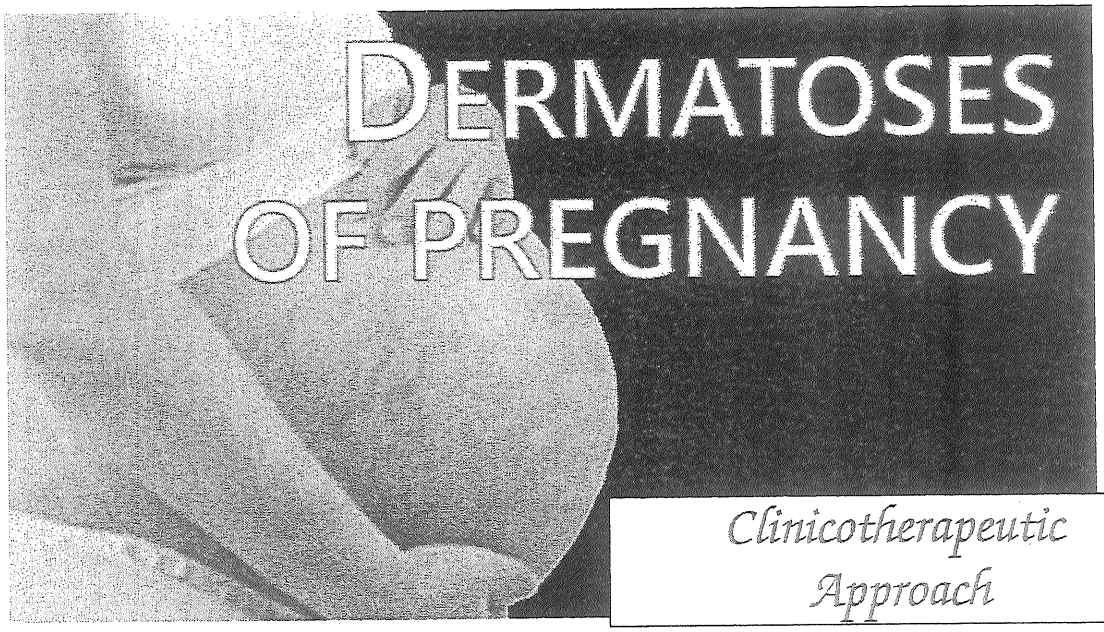
Treatment

1. Fetoscopy and prenatal biopsy at 18-20 weeks gestation for electron microscopic examinations to show any defects of basal keratinocytes, tonofilaments, hemidesmosomes, anchoring filaments or fibrils.
2. Prevention or control of friction or trauma with nutritional supplements. < Vits, Zinc (why ?? Oes. Stricture)
3. Topical antibiotics.
4. Vit. E orally.
5. Phenytoin in RDEB: not effective. (Mechanism → -- Collagenase). (غير فعال)
6. Systemic steroids.
7. Surgical intervention to correct disfigurement.
8. Minocycline, cyclosporin, retinoic acid, gene therapy.

9. Gene therapy: [For]

AR DEB:
- Introduction of NL Genes into Nucleus of epid. Stem Cells → Formation of NL proteins.
- disadv. Gene ± degraded, Neutralized by Abs or Shed inside a differentiating KCs.

AD-DEB:
→ Inactivation of Mutant Genes.
بدل ما ندخل جين طبيعي هنوقف عمل الجين الغير طبيعي



DERMATOSES OF PREGNANCY

Clinicotherapeutic Approach

Dr.Hany Abo Al-Wafa, MD

Definition

Cutaneous changes secondary to pregnancy related hormones as:

- **Estrogen**
- **Progesteron**
- **HCG &**
- **↑↑levels of Pituitary, Thyroid & Aadrenal glands Hormones**

Pathogenesis..
Basic Immunology

Types Of WBCs

Granular

(Cytoplasmic Grs. &segmented Nucleus, NEB)

- Neutrophils
- Eosinophils
- Basophils

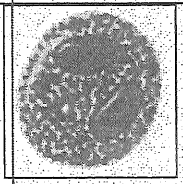
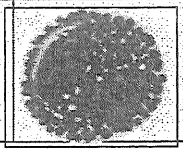
Non Granular

(Neither Granules Nor Nuclear Segmentation)

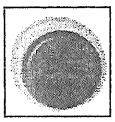
- Monocytes
- Lymphocytes

(Mononuclear Cells)

Granular Leukocytes

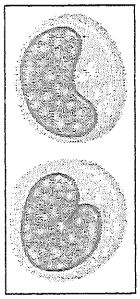
Type% of total WBCs	Diagram	Nucleus	Granules	Main targets
Neutrophil (62%)		Multilobed	Faint Pink.	- Phagocytosis and - Degranulation→Antimicrobial peptides (Myeloperoxidase, , defensins, cathepsin G, Alkaline phosphatase, collagenase, lactoferrin and cathelicidin)
Eosinophils (2.5%)		Bilobed	Pink	- Degranulation→ proteins (ECP, MBP, Cytokines, GFs) → attack parasites & Modulate allergic inflammatory responses
Basophils (0.5%)		Bi or Tri-lobed	Blue	-Release histamine, Heparine → role in parasitic infestation and Allergic diseases

Non-Granular Leukocytes (Mononuclear Cells)



Lymphocytes

Monocytes

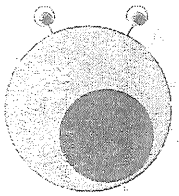


T-Lymphocytes

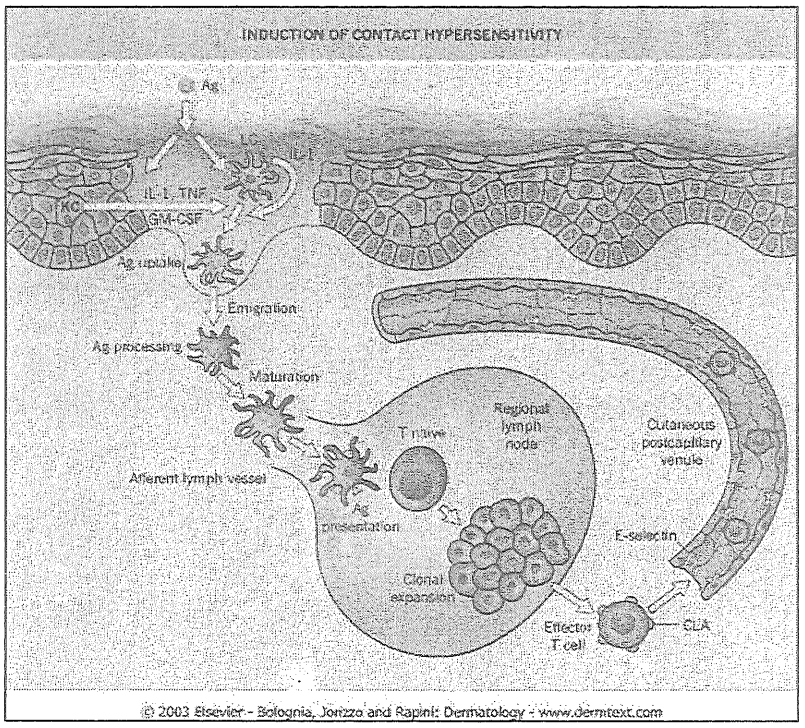
- Naïve (T0)
- Helper (CD4)
- Cytotoxic (CD8+)
- Others *(Memory, NKT, Mucosal associated&γδ T cells)*

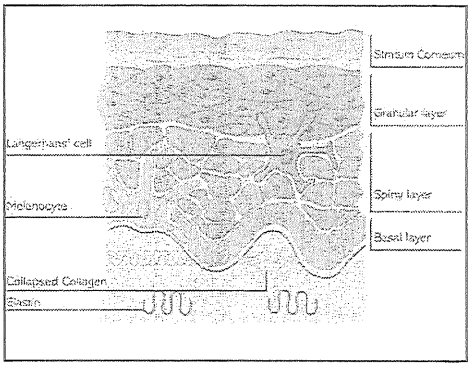
B-Lymphocytes

Plasma Cells



Langerhan's Cells+NaïveTC → TC differentiation



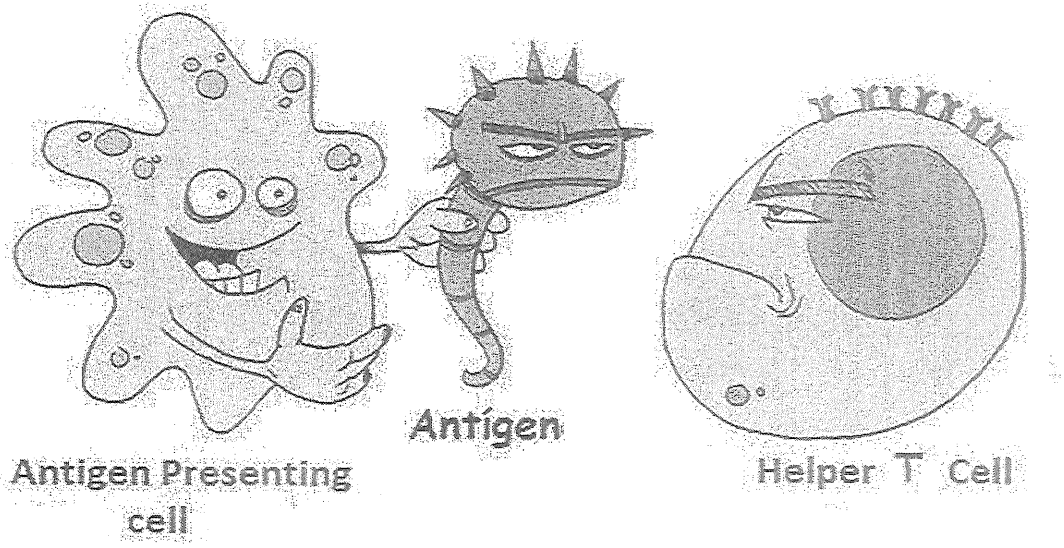


APCs+Naïve T cells (T0)

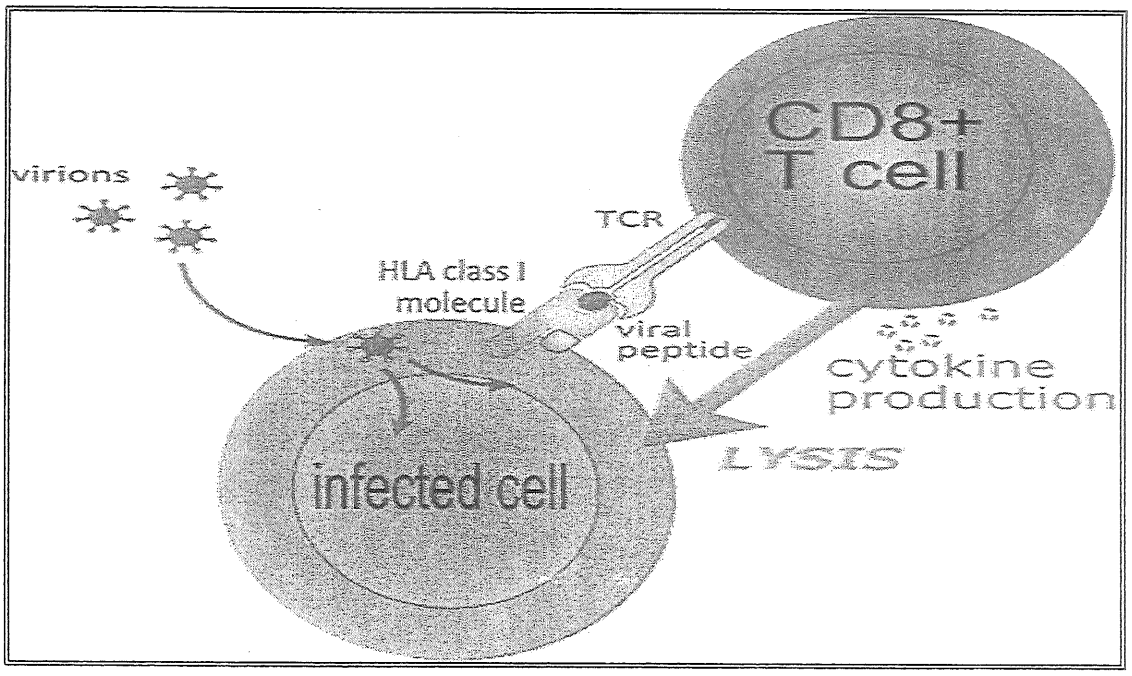
- T-Helper (CD4, Th0)
- Cytotoxic (CD8)
- Others: Treg, Memory, NK

- **Th1**
- **Th2**
- **Th17**

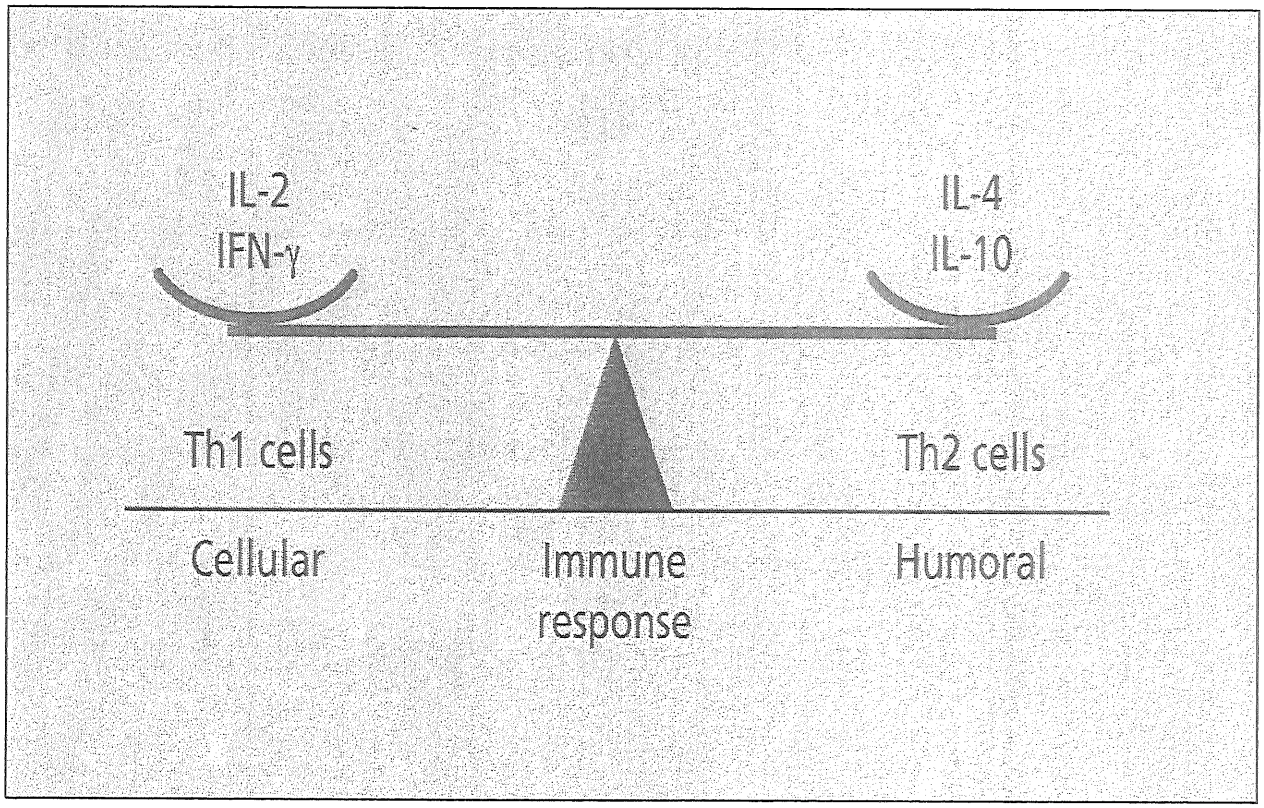
Interaction Between APCs &NaïveTC



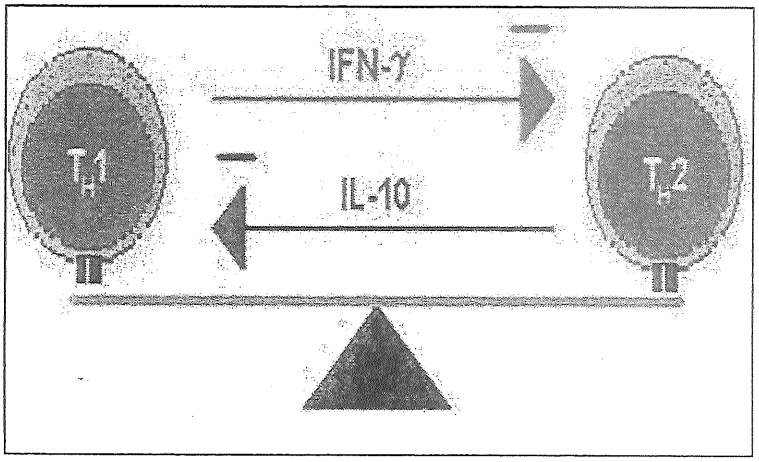
CD8+ interact with non Professional APCs (virally infected and Tm cells) which express antigens on their MHC-I

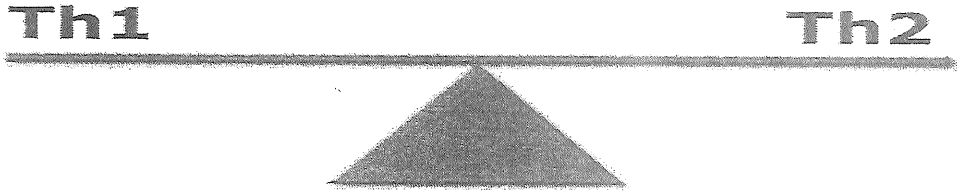


Th1 *Vs* Th2

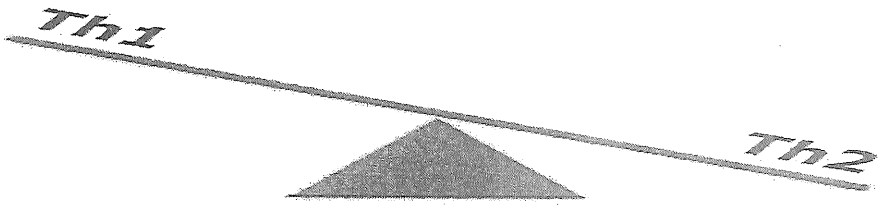


Th1 &Th2 Conflict

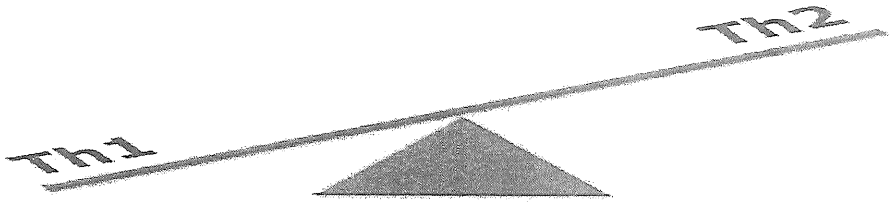




Balance=Normal



Psoriasis, Tuberculoid Leprosy



Pregnancy, Atopy, SLE,Lepromatous Leprosy

Classification of Dermatoses of Pregnancy

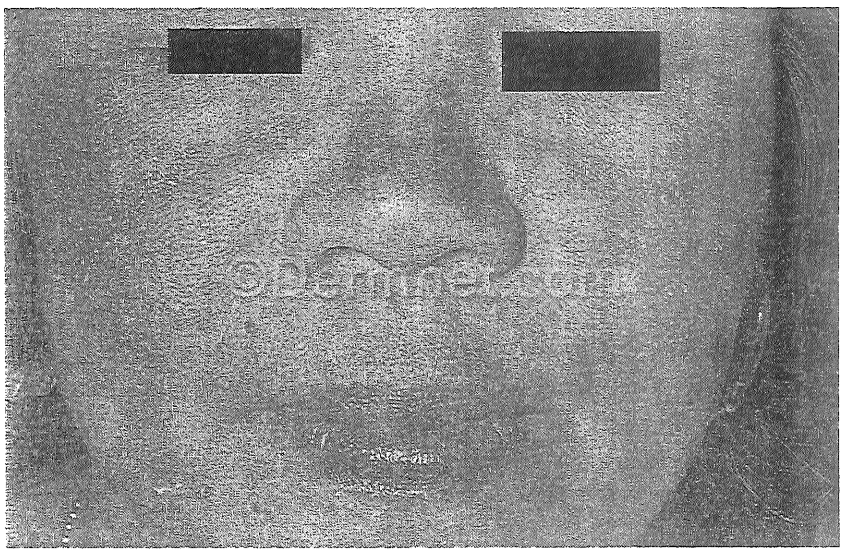
- Physiological changes during pregnancy
- Dermatoses Exacerbated or Improved during Pregnancy
- Specific Dermatoses of Pregnancy

I- Physiological Changes during Pregnancy

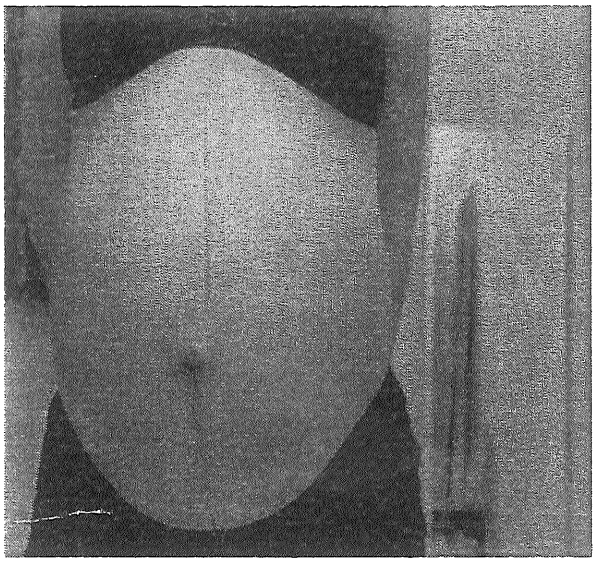
- Most of them are spontaneous and may resolve after pregnancy

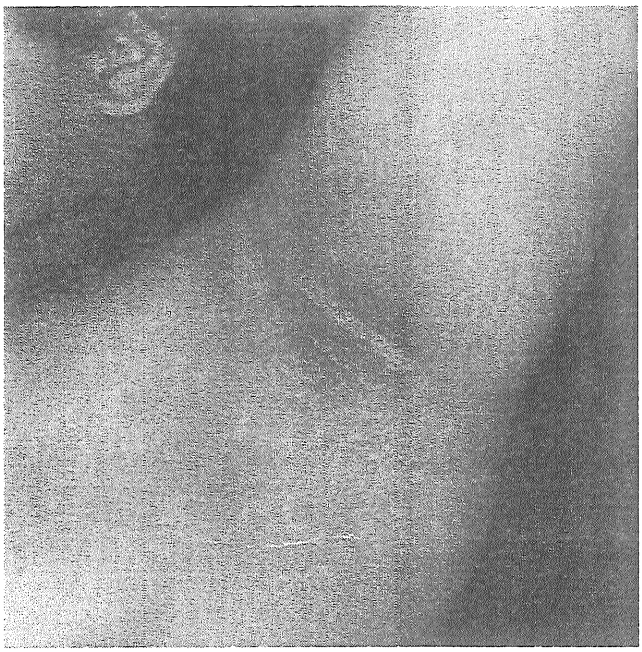
Hyperpigmentation

Melasma (chloasma)

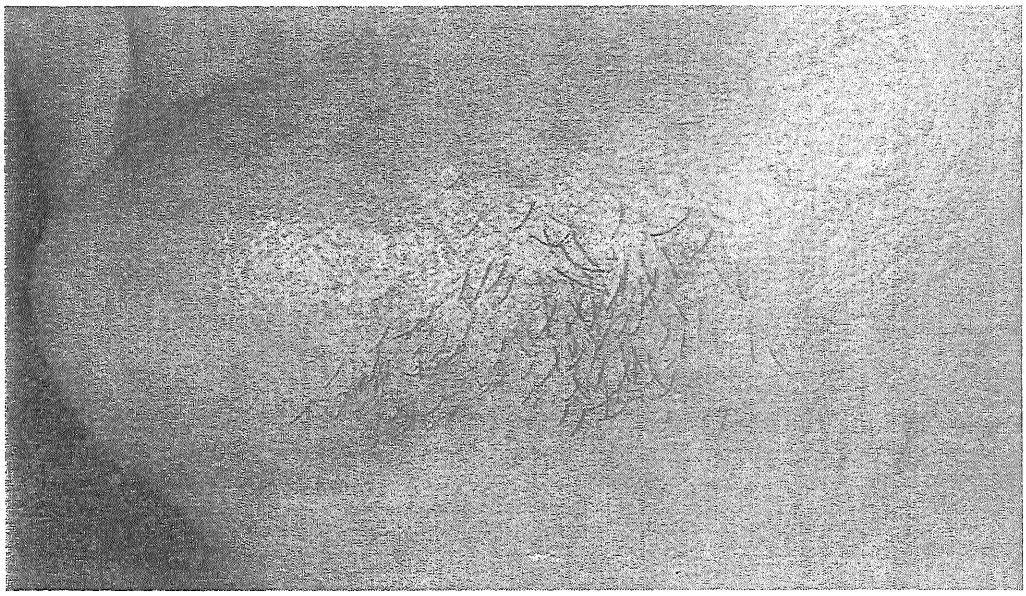


Linea nigra and Flexural Hyperpigmentation



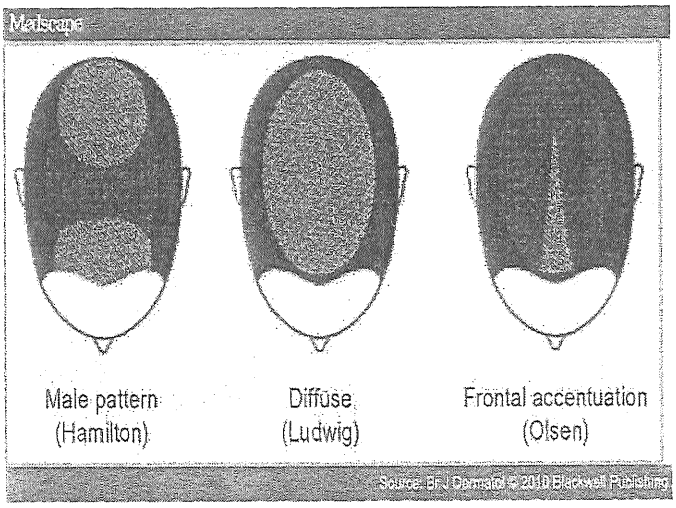


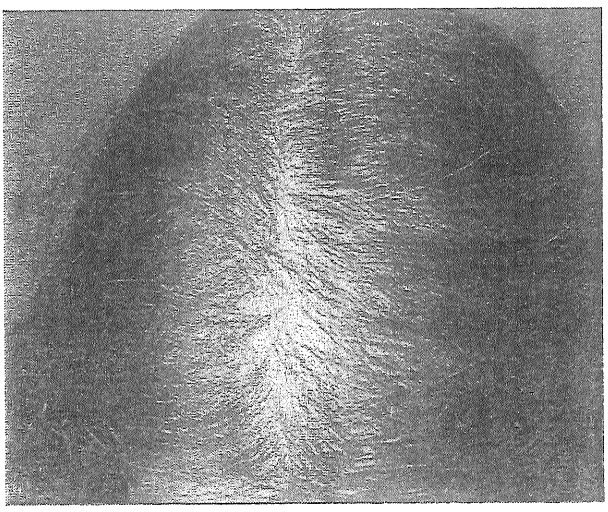
Hirsutism



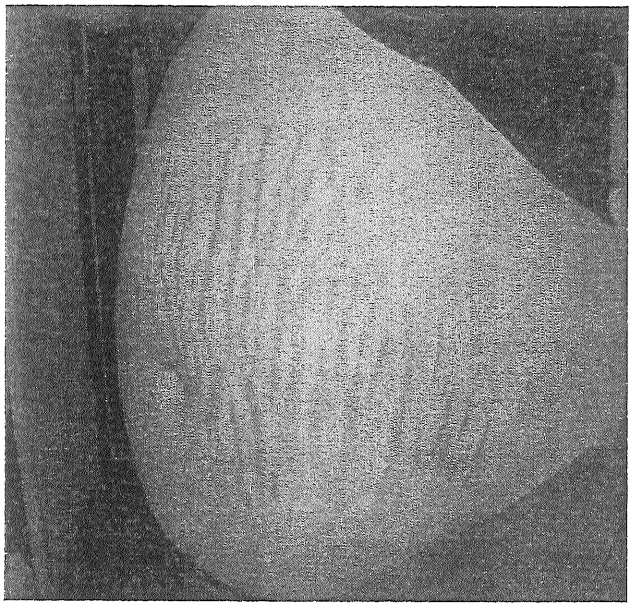
Postpartum Telogen Effluvium

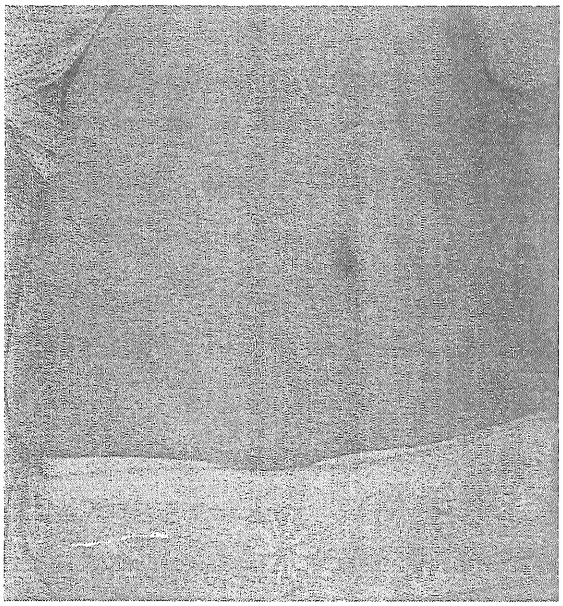
NB: AGA Shows preservation of anterior Hair Lines





Striae Rubra/Alba





Treatment of striae, an evidence based *(BJD, 2014)*

I- General Rules

- There is neither accepted nor ideal modality
- Striae rubra are resposnsive to therapy while alba rarely responding
- There is no prophylctic TTT for pregnancy associated striae, while Avoidance of rapid weight loss or gain may help prevent puberty and obesity associated striae

II- Medical TTT

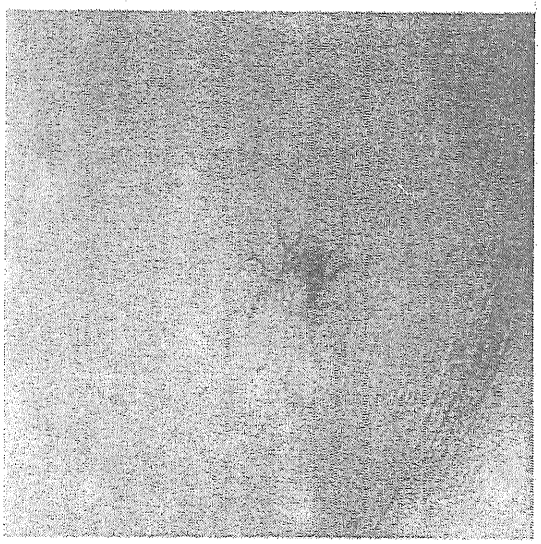
Topical Retinoids (effective), Topical Vit.C, some herbals (cocoa butter).

III- Physical Methods

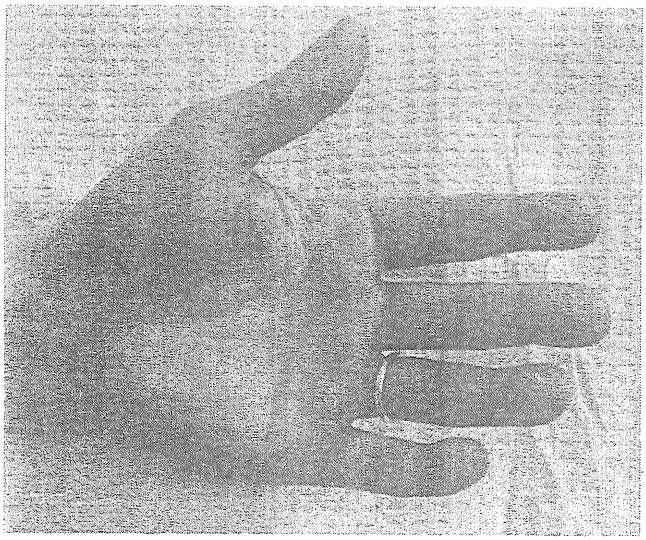
TCA and glycolic peel, PDL laser, CO2 laser, and Fractional laser.

Vascular changes

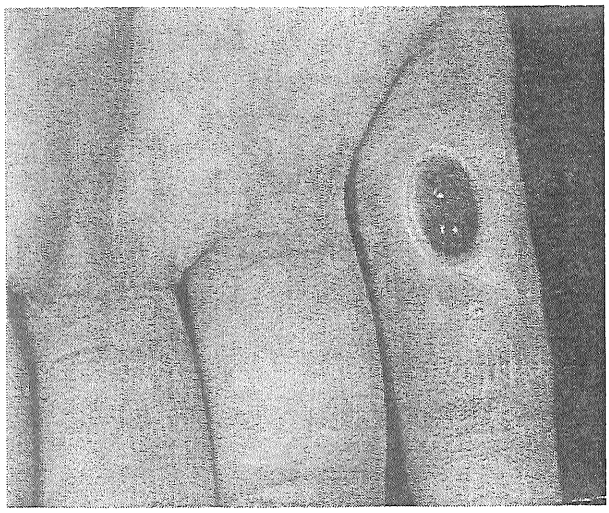
Spider Angioma

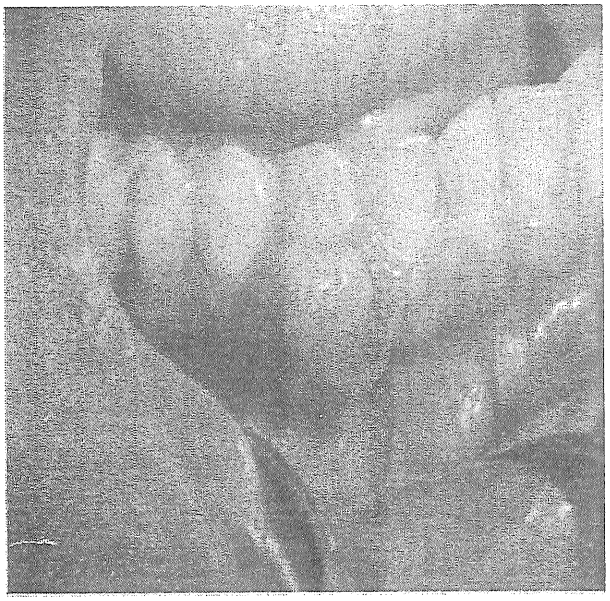


Palmar Erythema

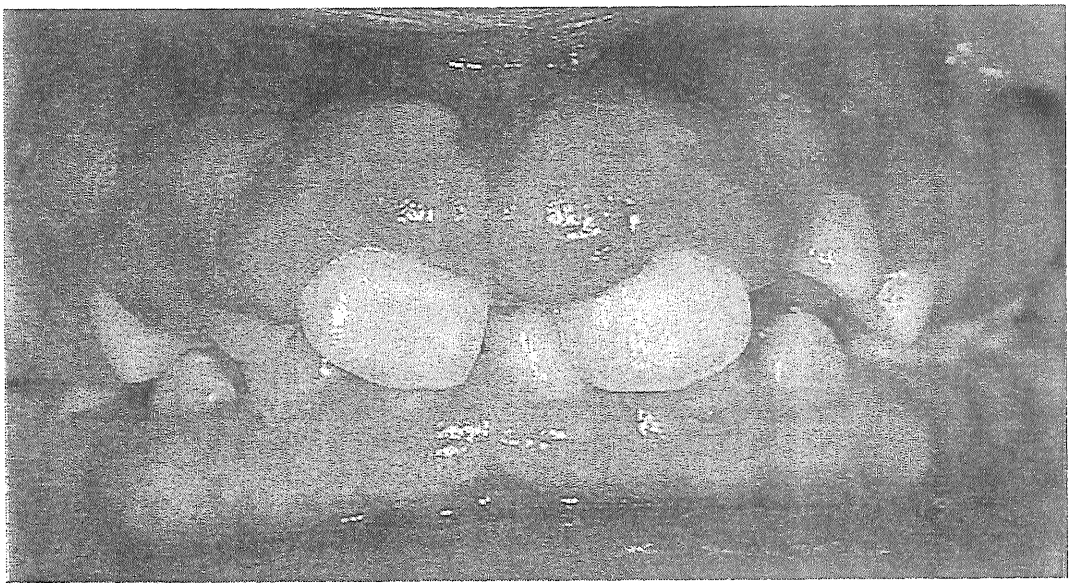


Granuloma Gravidarun (Pregnancy tumor)





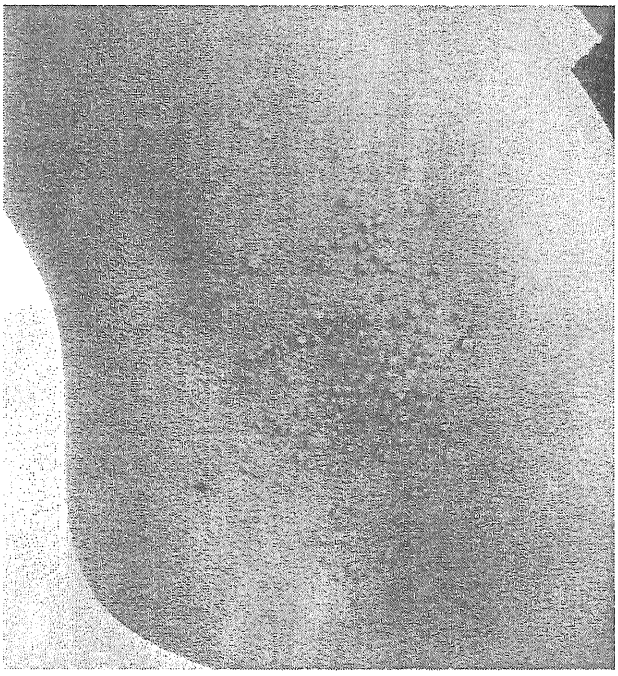
Gingival Hyperplasia

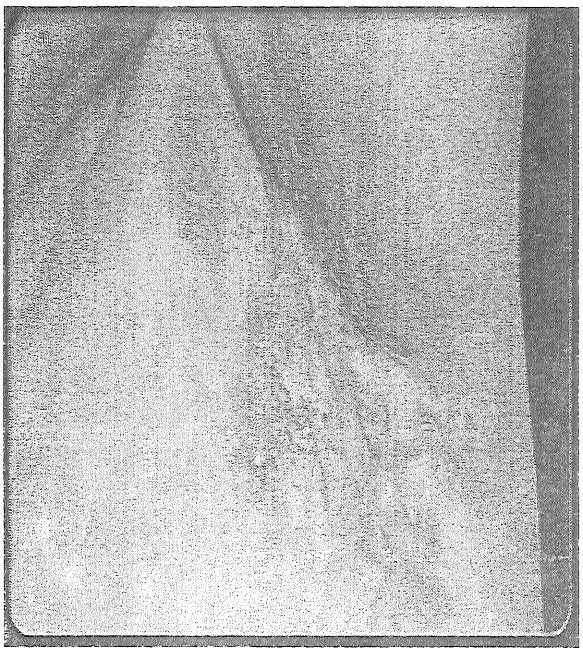


II- Dermatoses exacerbated or Improved during pregnancy

- Generally speaking; the disease improved may also exacerbate (no rule).
- **Th2 Mediated diseases:** will Exacerbate eg. Atopy, SLE
- **Th1 Mediated diseases:** Will improve eg. Psoriasis

Diseases that may improve are: Psoriasis, Fox-Fordyce & Hidradenitis

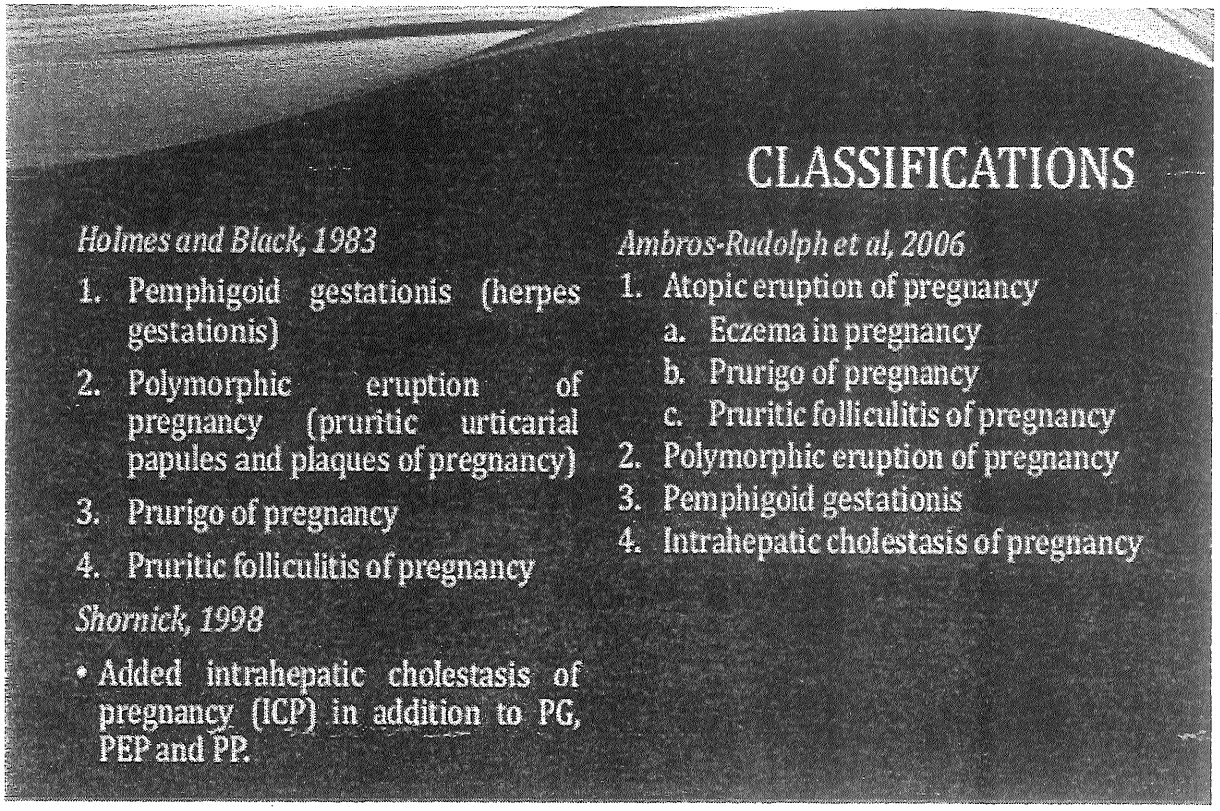




III- Specific Dermatoses of Pregnancy

- **Represent a heterogeneous group of severely pruritic inflammatory dermatoses associated exclusively with pregnancy or *the immediate postpartum period*.**

- **These dermatoses have been reclassified recently.**



Recent classification (JAAD,2006,Debated)

- Pemphigoid (Herpes) Gestationis (HG/BG)
- Polymorphic eruption of pregnancy (PEP)(*Old name:* PUPPP)
- Intra-hepatic cholestasis of pregnancy (IHCP) (Prurigo Gravidarum).
- Atopic Eruption of pregnancy (AEP) (*Old names*: Prurigo of pregnancy, and Pruritic folliculitis of pregnancy).

Clinical Approach, Itching during Pregnancy

Itching without Rash	Itching with Rash
➢ Physiological Pruritus (50%)	- PEP/PUPPP
	- HG/BG
➢ IHCP	- Atopic Eruption of (AEP,Prurigo of pregnancy)

Dermatoses Not Associated with Rash

Intrahepatic Cholestasis of Pregnancy (Prurigo gravidarum, IHCP)

- **Def.:** Hepatic condition that occurs during 3rd trimester and characterised by pruritus +/- jaundice(10%)
- **Incidence:** 3rd most common dermatosis of pregnancy.
- **Onset:** 3rd trimester (but +/- early at 8th week)
- **Pathogenesis:** ↓ Bile acids excretion → ↑ serum level → Cross the placenta → cause fetal anoxia & cardiac depression

C/P & Criteria

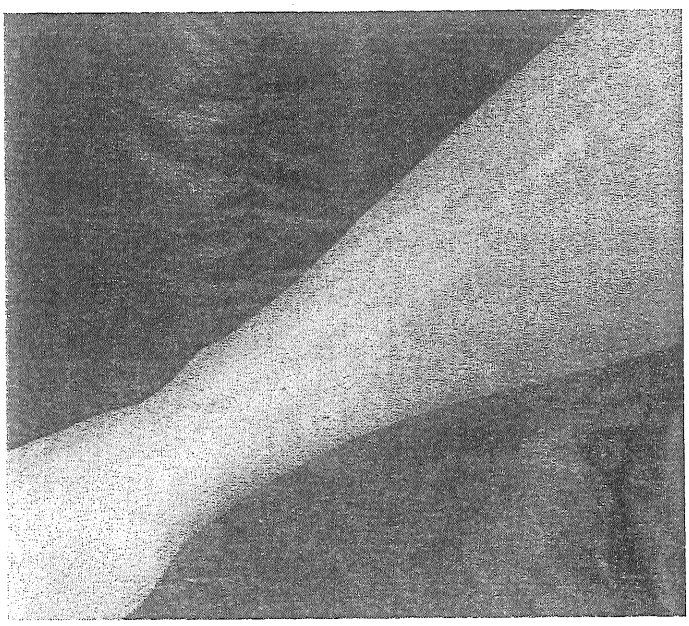
- **Generalised Pruritus:** ↑ ↑at night, involves face, palms and soles

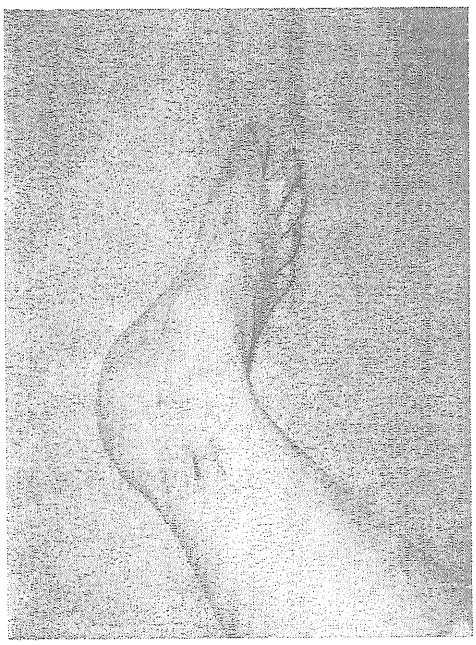
- **NO 1ry Skin Lesions** (only 2ry excoriations).

- **Jaundice** : 50%

- **Biochemical Abnormalities:**
  - ↑bile acids(الاهم عالاطلاق) (total, cholic acid&chenodeoxy cholic)
  - SGPT (مهم)و↑total bilirubin, ↑SGOT
  - Alk.Phosphatase

IHCP





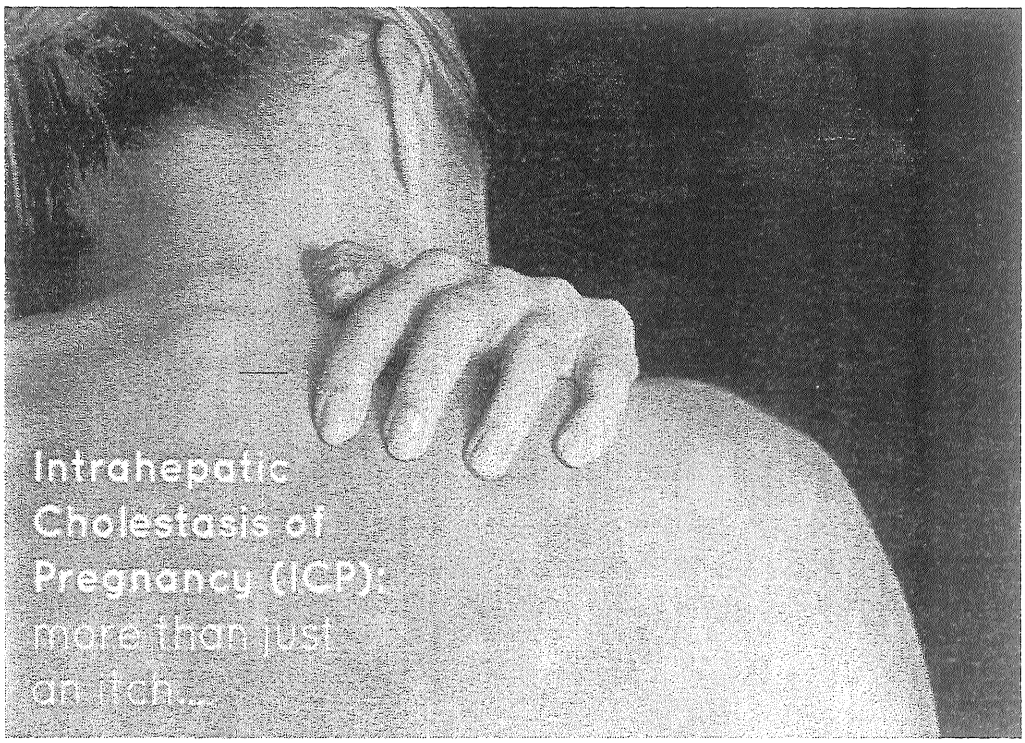
- **Resolution:** with delievery

- **Recurrence:** with subsequent pregnancy and OCPs.

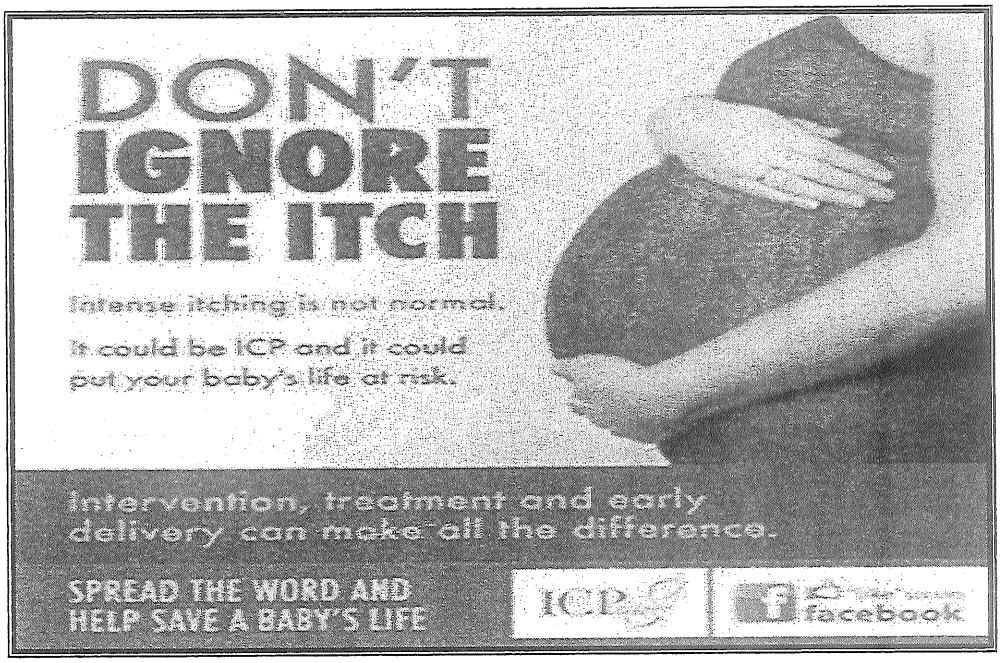
- **Complications**

  - **Maternal:** steatorrhoea,↓ Vit.K absorption, Gallstones, HEMORRHAGE

  - **Fetal:** IC hemorrhage, distress, stillbirth (1-2%),Cardiac Depression.



ICPcare™



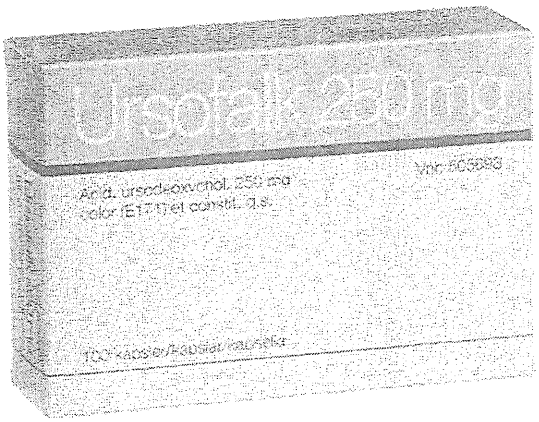
IHCP,Treatment

Bed rest , low fat diet

Vit. K ,induction at 38 Ws gestation

Ursodeoxycholic acid (15mg/kg)

Category B



Dermatoses Associated with Rash

Polymorphic Eruption of pregnancy (Pruritic Urticarial Papules and Plaques of Pregnancy) (PUPPP)

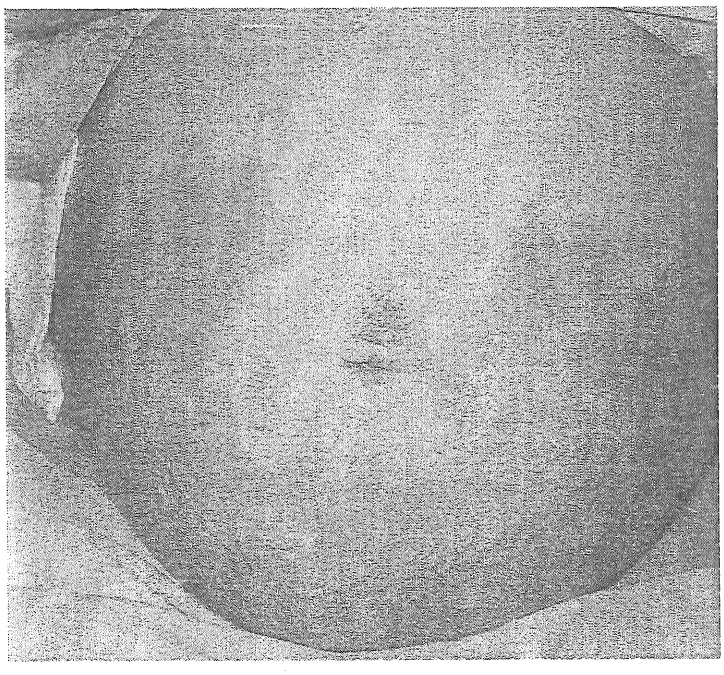
- **Incidence:** the 2nd most common specific dermatosis of pregnancy
- **Etiopathogenesis:** ??, may be related to rapid and marked abdominal distension→ CT damage→ inflammation→ PUPPP

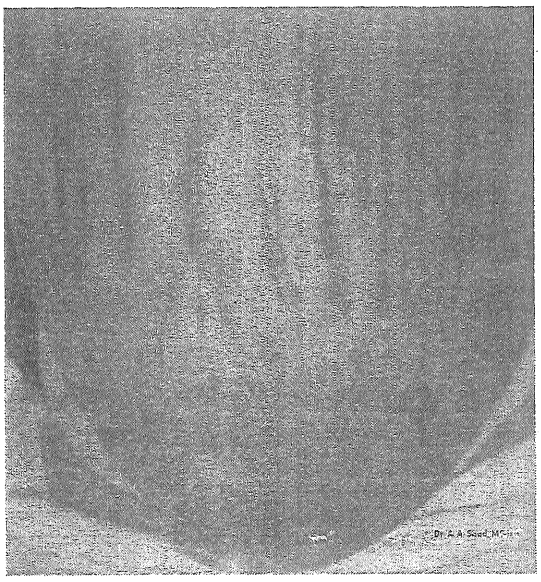
- **Risky Patient:** primigravida, 3rd trimester,twins, overweight baby and polyhidraminos.

- **Onset** :3rd trimester or immediate post-partum

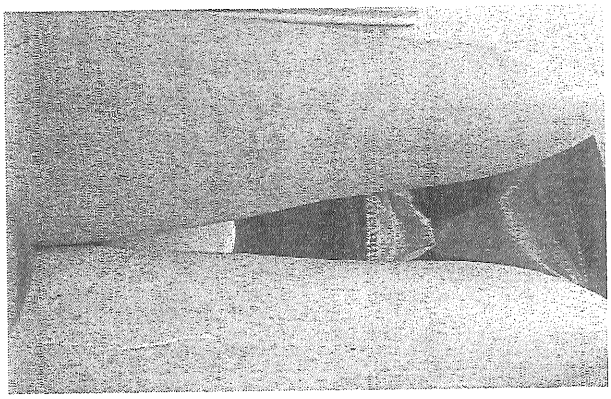
- **C/P:** severly itchy, PUPP (polymorphic lesions):Eczematous, targetoid lesions, vesicles (BUT NO BULLAE). Lesions start at STRIAE, then spread

PUPPP





PUPPP



- **Resolution**: few days after delievery
- **Recurrence :** NO
- **Complications** :NO
- **Treatment:** (symptomatic)
  - Antihistamines
  - Topical Cs
  - Systemic Cs
  - NB-UVB

Pemphigoid (Herpes) Gestationis (PG)

- **Def.:** Self limiting autoimmune bullous disorder of mainly late pregnancy or postpartum.

- **Incidence:** Rare

- **Onset:** 3rd trimester or even postpartum.

NB: There is often a relative quiescence in late pregnancy, followed by a flare at the time of delivery or in the immediate postpartum period in 75% of cases.

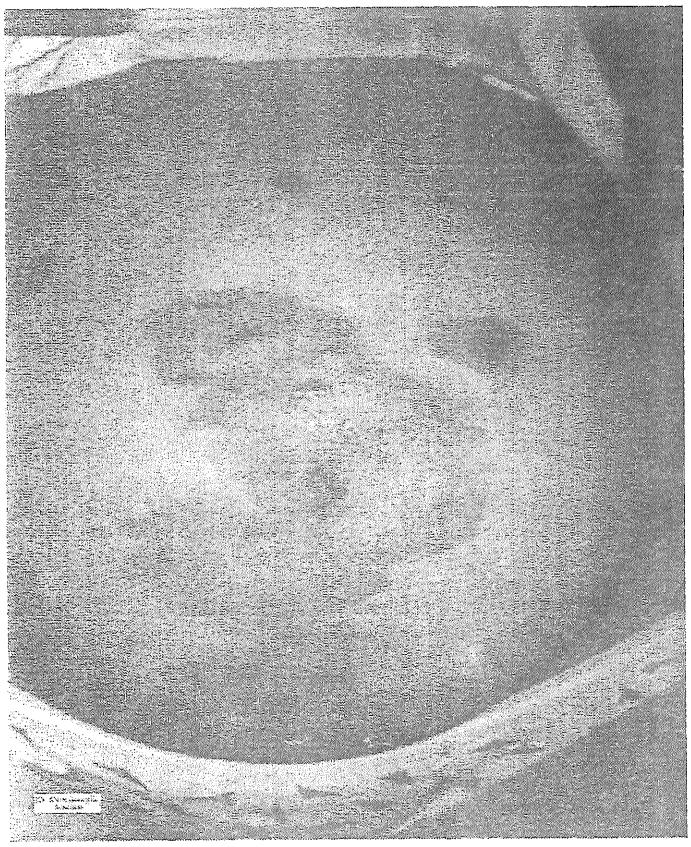
- **Etiopathogenesis:** Abnormal expression of class II HLA DR3, DR4 (paternally derived) at chorionic villi of placenta→ immune response initiation against placental BMZ Ag (HG Ag)→ IgG1 autoantibodies→ cross-react with cutaneous BPAg2 (180-kd) and BPAg1(230-kd) at BMZ

CP

- **C/P:** PUPP like lesions, targetoid lesions, usually start *PERIUMBILICALLY* → involve trunk,back,buttocks and arms →large, tense bullae+/-annular configuration

- **NB:**
  - There is sparing of Acral parts and MM(20 % only)
  - Sometimes NO blisters, only erythematous plaques and targetoids.

PG



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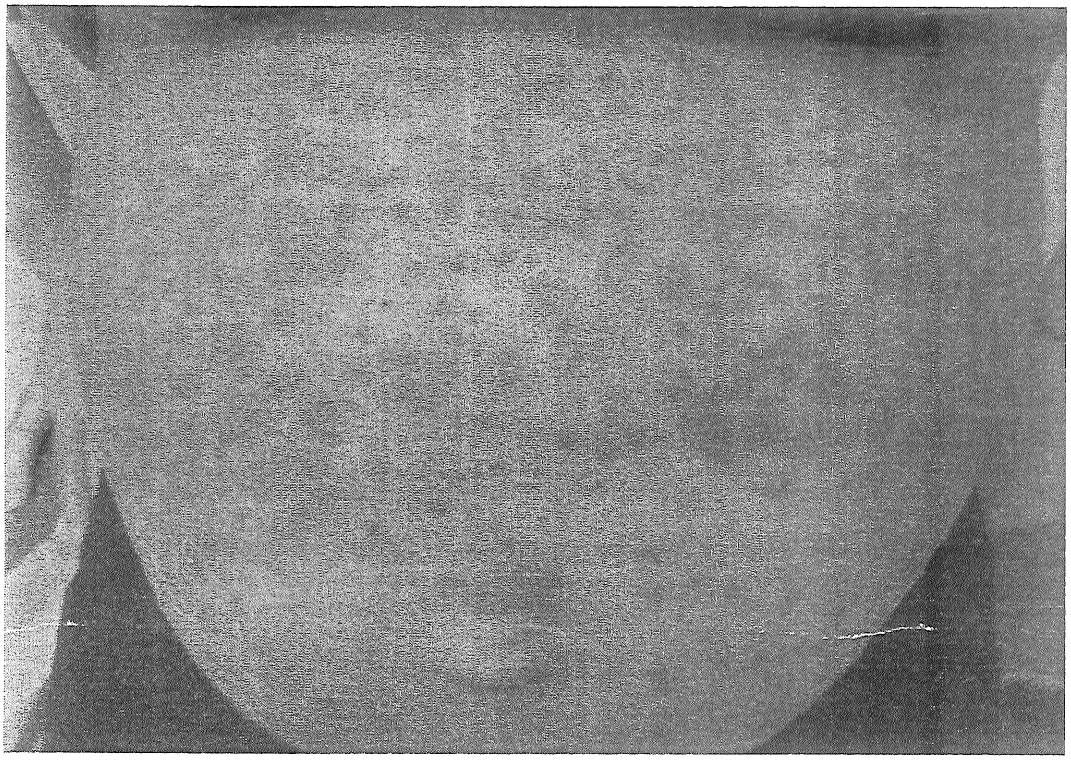

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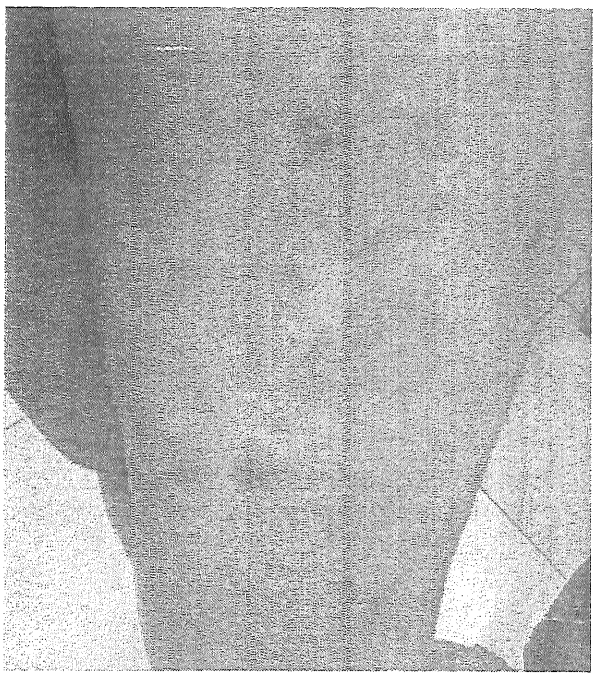

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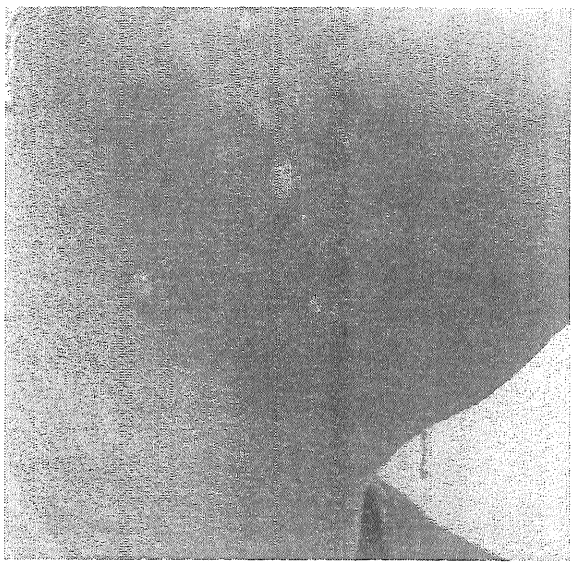


- **Resolution:** Postpartum, (Ws-Ms)

NB: Some cases has protracted course called chronic PG while others develops classical BP).

- **Recurrence:** with subsequent pregnancy, OCPs, vesicular mole or choriocarcinoma.

NB: '*Skip pregnancies*', however, have been reported (8%) and were attributed to a male consort (قرين) change or expression of identical HLA-DR antigens by mother and fetus.

- **Diagnosis:**
  - **HP**: subepidermal blisters with eosniophilic infilt.
  - **DIF**: Linear C3, IgG at L.L of BMZ.
  - **IIF:** IgG autoantibodies against BP Ag2 and BP Ag1

- **Complications:**
  - **Maternal:** BP (some case)
  - **Fetal**: PG, Prematurity, LBW, Neonatal BP (10%, due to maternal transfer of autoantibodies).

- **Treatment:**
  - **Mild HG:** Antihistamines , Dermovate
  - **Severe HG**: Systemic Cs.

PUPPP *Vs* PG

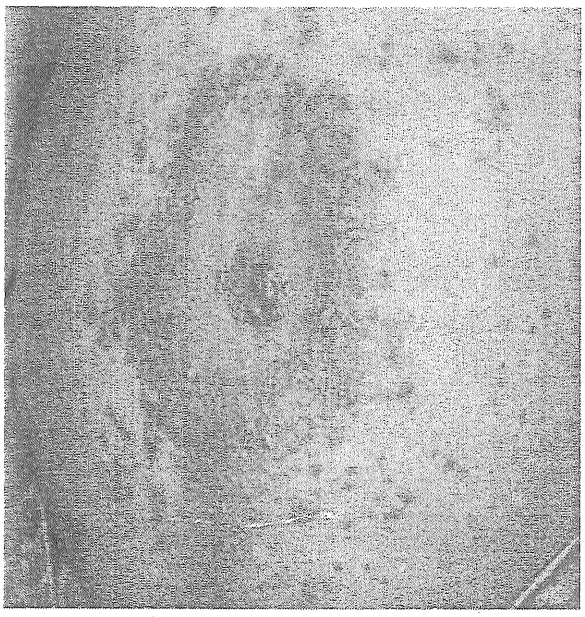
- **Both:** at 3rd trimster or postpartum

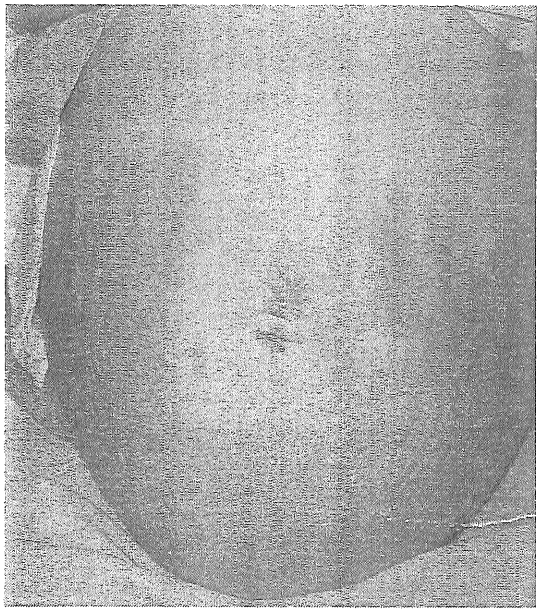
- **PUPPP:**
  - Primigravida
  - At striae.
  - Lesion may be targetoid or vesicular (NO BULLAE).
  - NO complications
  - NO recurrence

HG:

- Sarts Periumblically
- PUPP then become bullous.
- Lesion may be targetoid or remain NON BULLOUS.
- Complicated
- Recurrent

So the periumbilical area is considered as a land- mark in diagnosis of both PUPPP (free only striae) & HG (involved)





Atopic Eruption of Pregnancy (AEP) (Prurigo of pregnancy)

- **Incidence: AEP is the most common dermatosis of pregnancy, accounting for 50% of pregnancy specific dermatoses**

- **About 20% of women experience an exacerbation of pre-existing eczema in pregnancy, whereas 80% experience atopic skin changes for the first time or after a long remission (for example, since childhood)**

- **Etiopathogenesis:** immunosuppression with predominance of TH2.

- **Onset:** Before the 3rd trimester (بدري عن باقي الانواع)

- **Types :**

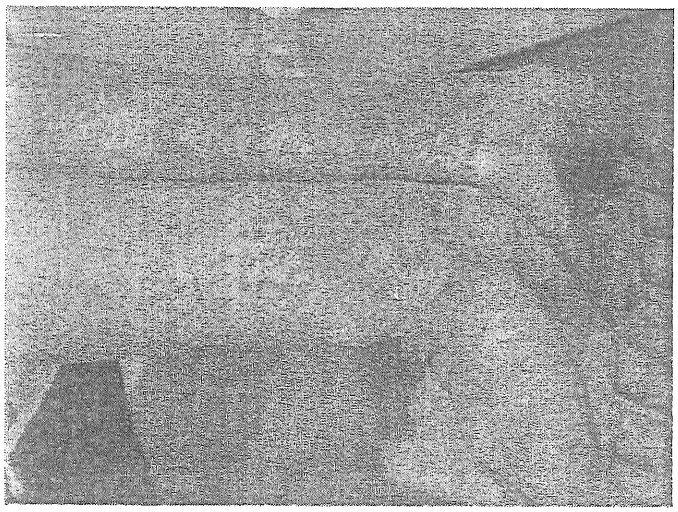
  - **Eczematous type (papular dermatitis of pregnancy)(2/3 cases):** 1st& 2nd trimester, eczematous changes affecting typical atopic sites such as the face, neck and flexures

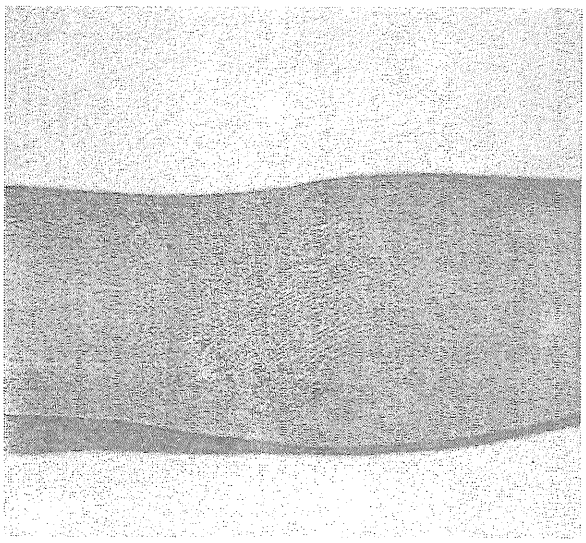
  - **Papular type (Prurigo of pregnancy) (1/3 cases)**

  - **Pruritic folliculitis of pregnancy.**

- **Resolution:** Postpartum
- **Recurrence :** With subsequent pregnancy
- **Complications:** NO maternal, may be fatal Atopy

AEP (Eczematous)



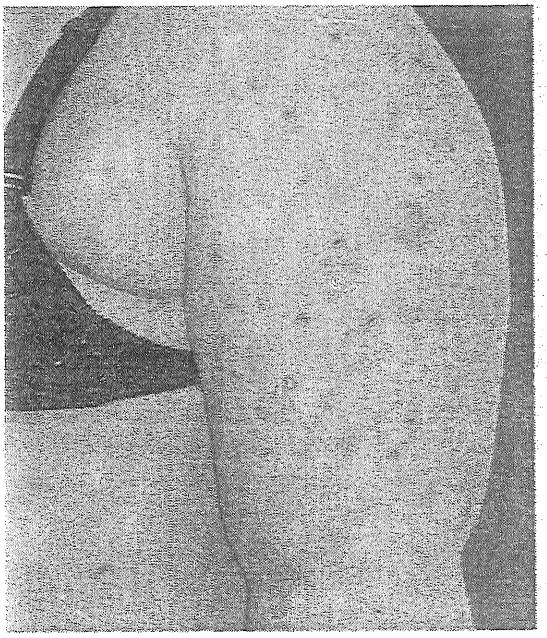


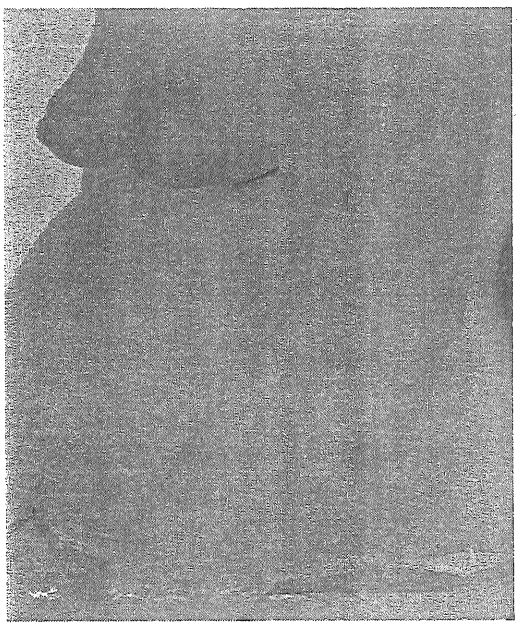
Prurigo of pregnancy
(Not Prurigo Gravidarum)

Itchy, Excoriated, Papules and Nodules (prurigo nodularis like), at Extensors and Trunk

- **Onset:** 2nd or 3rd trimester
- **No** complications
- +/- Recurrence
- **Symptomatic** treatment

AEP (Papular/Prurigo of pregnancy)



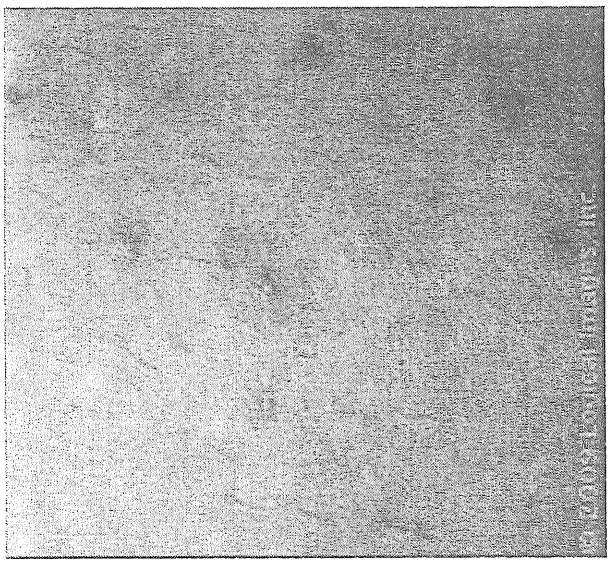


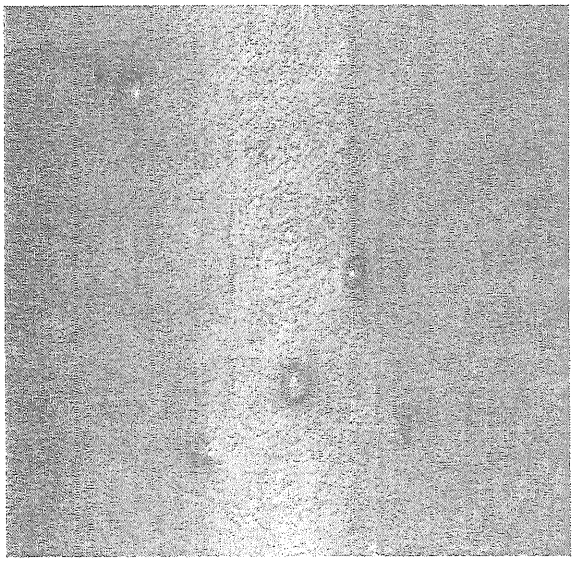
Pruritic folliculitis of pregnancy

Itchy, follicular papules and Pustules at Trunk and Extremities (Acneiform like eruptions)

- **Etiopathogenesis:** a form of hormonally induced acne, similar to steroid acne
- **Onset:** 2nd or 3rd trimester
- **No** complications
- **+/-Recurrent**
- **TTT:** Topical Cs, antihistamines or UVB

Pruritic folliculitis of Pregnancy





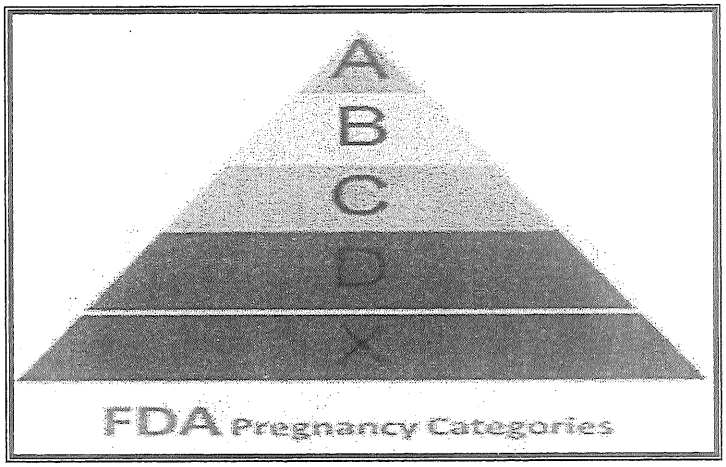
Other Dermatoses: Unclassifies

- Impetigo herpetiformis (pustular Psoriasis of pregnancy)
- Autoimmune progesterone dermatitis
- Linear IgM dermatosis (Non specific dermatosis, characterized by:follicular papules&pustules that show Linear IgM by DIF

Autoimmune Progesterone Dermatitis

- Though, non specific for pregnancy , but it may appear for first time during it
- Eczematous, urticarial&EM-like rash during Luteal phase of cycle
- Diagnosis: Intradermal injection of progesterone→ urticaria within 30 mins. Or Erythematous induration within 1-2ds
- TTT: Stop ovulation (Estrogen only pills, Tamoxifen&Danazol)

Dermatological Drugs & Pregnancy



FDA Categorization of Drugs during Pregnancy

Category	Definition	Animal studies	Human studies
A	No risk in controlled studies	-ve	-ve
B	No proven risk	-ve	No data
		+ve	-ve
C	Risk can't be ruled out	+ve	No data
		No data	No data
D	Evidence of risk	-ve or +ve	+ve
X	Sure risk, Absolute contraindication	+ve	+ve

FDA Categorization

FDA pregnancy drug class

Class	Clinical implication	Example
A	No risk to fetus	Vitamin B6
B	No evidence of risk	Brimonidine, azithromycin, erythromycin, tobramycin
C	Risk to fetus cannot be ruled out	Ciprofloxacin, other glaucoma medications, corticosteroids, dilating agents
D	Risk to fetus, but benefits may outweigh risk	Tetracycline, doxycycline
X	Definite risk; Avoid	Misoprostol

Source: Food and Drug Administration

Antihistamines & Pregnancy

- **Sedating Antihistamines:**

All are category (B) except hydroxyzine (Atarax) and Doxepine are (C).

- **Non sedating Antihistamines:**

All are category (B) except fexofenadine and desloratadine are (C)

However; cumulative experience with sedating types are greater, so chlorpheniramine (Avil, anallerge) is the safest during pregnancy

Systemic Cs & Pregnancy

- **Category:** C
- **1st trimester:** Cleft Palate
- **Others:** LBW and Placental Calcification